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EVOLUTION OF RADIOLOGIC PHYSICS AS APPLIED TO ISOTOPES

JANEWAY LECTURE, 1950*

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WHEN I first set foot in this great country twenty-eight years ago, I had many ambitious aspirations, but my dreams never went so far as to imagine that I should sometime be invited to deliver a lecture of the importance of the Janeway Lecture to a great scientific body. I deeply appreciate the honor. Dr. Henry Harrington Janeway died a year before I arrived in the United States, but his successful efforts to place the medical application of radium on a sound basis had left a deep imprint which could then and still can be felt everywhere.

I shall never forget my first visit with Drs. Quick, Failla and Quimby at the old Memorial Hospital on Central Park West, many years ago. There the work in radiation therapy was imbued with Janeway's spirit of scientific investigation, as Edith Quimby[13] so aptly expressed it. The close cooperation between the Departments of Physical Research and of Clinical Radiology, which stemmed from Janeway's ideas, made a deep impression on me. The application of these ideas set a pattern for our own and for many other institutions which has borne rich fruit.

Janeway was one of those few great surgeons who became interested in physics simply because he saw the need for it in the correct handling of radium. He took night courses in physics and became quite proficient as a physicist himself, and he had the vision to offer a part-time position in his hospital to Gioacchino Failla, who was then a young graduate student in physics at Columbia University. I need not enumerate the accomplishments which resulted from this association, for you are all familiar with the great influence that the school of Janeway, Quick, Failla, Quimby, Marinelli and their associates has had on every phase of radiology.

As a physicist, I should like to call attention briefly to a rather curious parallel in Dr. Failla's and my own career. At just about the time that Failla accepted Janeway's offer for collaboration, I was offered a similar opportunity by Bernhard Krönig, who was also a great surgeon and gynecologist. Krönig, like Janeway, was deeply

* The fifteenth Janeway Lecture, delivered at the Thirty-second Annual Meeting of the American Radium Society, New York, New York, May 25–26, 1950.

interested in radium and first attracted Friedrich and, in turn, me to work with him on radiologic problems. Again, at the time when Failla did his beautiful work on radium dosimetry,[1] I was concomitantly measuring the isodose curves[3] around gamma-ray applicators and their combinations as they were being used in gynecologic practice at the University Women's Hospital in Freiburg i. Br.

All that was more than thirty years ago and, in the intervening years, many other physicists have entered this field of medical radiologic physics. To me it is still one of the most fascinating fields of applied science and research.

In evaluating the present status of radiologic physics, it is instructive to look back on some of its historic developments. This is especially pertinent now, because there is a tendency on the part of some to believe that the remarkable work concerned with the man-controlled release of atomic energy actually is the genesis of this branch of science, and to regard atomic physics as the alpha and omega of all that is significant in radiologic physics. However, when one takes even a cursory glance toward the past, it is evident that radiologic physics is by no means a new conception.

The discovery of the x-rays by Wilhelm Conrad Röntgen in 1895 marked a fundamental milestone in the history of physics and of medicine as well, and focused attention on the relationship between them, which has become constantly closer ever since. During my student days my teacher, Walther Friedrich, himself a pupil of Röntgen, aroused in me a consuming curiosity as to the personality and scientific accomplishments of Röntgen. This interest assumed for me the proportions of an avocation and culminated in later years in several historical books about the discoverer and the discovery of the x-rays.[5,6,7] The most impressive fact brought out in these studies was the dramatic challenge this discovery by an academic physicist offered to the medical profession.

Röntgen's great discovery might have been confined to his own quiet laboratory in Würzburg and to a few other university laboratories for a long time, perhaps for years if, in his original publication, he had chosen to confine his observations on the "penetrating rays" to dry absorption data on inanimate material, such as aluminum, glass or hard rubber. But, when mailing reprints of his preliminary paper, he wisely included the "ghostly" picture of the bones of his wife's hand, and it was this picture that captured the imagination of the scientific profession and the lay public throughout the world. This was the experiment, of all the experiments he described, which was reproduced almost immediately by physicists everywhere who had a Geissler-Crookes tube and an induction coil or a static machine. Medical men and laymen, too, were quick to see the importance of the discovery as a new instrument for the study of anatomic structures and pathologic changes. The tremendous scientific activity stimulated by this discovery in physics is evident in the fact that physicians and physicists published fifty books and more than a thousand papers on the x-rays within the first year after Röntgen's initial report.[5,6,7]

Röntgen's discovery of the x-rays was followed one year later by Becquerel's discovery of radioactivity, by J. J. Thomson's isolation of the electron in 1897 and the discovery by the Curies of polonium and of radium in 1898. The details of these events were presented to you two years ago, at the fiftieth anniversary of the discovery of radium, by Edith Quimby[14] in her splendid address, "Fifty Years of Radium." These great discoveries, and equally important contributions by Rutherford, Planck, Bohr and Einstein brought new light and understanding concerning the structure of matter and radiant energies, and stimulated scientists all over the world to investigate the ramifications of these great discoveries and to add new observations of their own. In the early 1930's, these additions came thick and fast: J. Chadwick discovered the neutron, Irene

Curie and F. Joliot observed artificial radioactivity, Urey discovered heavy hydrogen and Anderson the positron. A few years later other physicists, Fermi, Hahn, Strassman, Frisch, and others, again made scientific history with their observations on uranium fission.

World War II lowered the curtain upon this remarkable four and one-half decades of international scientific progress, and the next scientifically significant step, the exploitation of the atomic chain reaction, was carried out in great secrecy. Even now, five years after the guns were silenced, a major part of scientific endeavor is still, or once more, shrouded in secrecy throughout the world.

What a contrast this is to the speed with which all the details of the discovery of the roentgen rays or of radium were disseminated and made available to everyone everywhere.[5,6,7] There is also another stark contrast. Röntgen, Thomson and the Curies worked alone and with primitive equipment when they made their great discoveries. Today large teams of research workers with magnificent and expensive equipment plunge forward into the uncharted fields of science. Nobody will deny the value of large-scale teamwork in attaining needed results under emergency conditions. That fact was most forcefully brought to the world's attention by the development of the uranium and plutonium bombs. Even so, the very foundation of that tremendous accomplishment was the modest announcement by Hahn and Strassman in 1939 that they had observed nuclear fission. While many of us are carried away by the dynamism of the ever accelerating attack by large research teams on scientific problems, there are also some who wonder whether the next fundamental discovery will come from their efforts, and if it does, whether it can be revealed to the world. Or could it be that it will come from the unpretentious laboratory of some present-day Röntgen or Curie? I rather favor the latter possibility.

In evaluation of this last half century of progress in unraveling the secrets of radiant and atomic energies, the radiologist and radiologic physicist are both greatly interested in and impressed by the interplay between pure physics and its application to medicine, which has contributed so greatly to the astounding development of radiology. As already mentioned, if the x-ray picture of Frau Röntgen's hand had not opened a wide vista for the use of x-rays in the study of anatomic and pathologic changes, the purely physical discovery might have been buried for some time in the oblivion of the physics laboratories. If those who were working in this field had not observed changes in their skin after prolonged exposure to roentgen rays and radioactive substances, their therapeutic value might not have been recognized for many years.

As it was, the demand by the medical profession for larger and more efficient equipment brought about developments in roentgen-ray machines, in radium applicators and radon plants, which would never have been supported by the modest laboratory needs and budgets of the physicists before World War II. This relationship between medical needs and physical developments runs like a golden thread through the whole fabric of the history of radiology. About twenty-five years ago, medical radiologists demanded roentgen-ray generators with higher voltages in order to produce radiations that could penetrate more deeply to treat internal lesions with greater dosages. This desire stemmed from the impression that gamma rays from radium, in properly constructed tele-applicators, apparently produced more satisfactory therapeutic effects than did roentgen rays of lower energies then available. Physicists and engineers, through painstaking work, produced such supervoltage machines for the medical radiologists.

In turn, these same machines served a purely physical but extremely useful purpose during World War II, where they were put to use in the detection of structural flaws in heavy shells, mines and other war

equipment. Once more, after the war, the supervoltage machines with all the improvements which had been incorporated in them through intense war research returned to the medical and biologic institutions to be put to work in the fight against cancer and allied diseases.

Truly the progress from Röntgen's first fist-sized x-ray tube and small induction coil to modern million volt transformers, Van de Graaff electrostatic generators, to 300 million electron volt betatrons, to giant cyclotrons and multibillion bevatrons is nothing short of fantastic. How quaint Röntgen's letter to a tube manufacturer sounds to us today when he complained that his tubes were good but too expensive. "I would like to ask," he wrote, "whether you are able to let me have the tubes for 20 instead of 30 marks." Imagine asking for a first class x-ray tube at a price of $5.00!

The fruitful results of this medical-physical relationship can be traced through many other phases of radiology, such as the construction of dosage instruments, protection survey meters, phototimers, Geiger counters and a host of others. Among these, none has been more fascinating to me than the efforts to develop proper dosage units, foolproof dosage instruments and radiation detectors for protection surveys against undesirable stray radiation. The solution of this problem, like all the others, required much effort and time. In this connection, it is interesting for me to recall the many days and nights I spent with my friends U. V. Portmann, V. Seitz, I. Beasley and Jack Victoreen, years ago, in constructing the condenser r-meter[4] and in applying the principles of the air-wall thimble chamber which Fricke and I[2] had developed to the commercial instrument which Jack Victoreen, with his inimitable skill, had designed. Today thousands of radiologists use this instrument routinely and as a matter of course, and as is to be expected, only a few know or think about the severe labor pains which accompanied its birth.

Twenty-five years ago, roentgen and radium therapy certainly was not yet an exact science. The roentgen-ray output of generators and tubes was erratic and often difficult to reproduce, and production of identical dosages with different machines was almost impossible. Radium dosages were expressed in various terms, mostly in exposures of so many milligrams or millicuries for a given time without precise knowledge of what happened to the rays when they were applied to tissue nor just how much radiation was being delivered to the part undergoing treatment. In recognition of this situation, the president of the Radiological Society of North America, Arthur Erskine, appointed in 1926 a committee of medical radiologists and radiation physicists to "study standardization of measurement of radiation." It was necessary to change the by-laws of the organization so that the physicists appointed to the committee could be admitted to associate membership in the society, marking a revolutionary step in admitting non-medical men to a purely medical society. The hearty cooperation of medical radiologists (notably of E. C. Ernst) and physicists (notably L. S. Taylor) on this standardization committee brought out significant progress in the measurements of radiation quality and quantity. These results were coordinated with similar work by other committees, and in 1937 the Fifth International Congress of Radiology, meeting in Chicago, finally adopted the roentgen as the dosage unit for radiation quantity and the half-value layer as the unit for radiation quality.

From this collaboration of physicians and physicists, several important developments ensued. A registry of radiologic physicists, qualified to assist medical radiologists with their problems, was created about fifteen years ago. This registry was taken over recently by the American Board of Radiology. Physicists also were appointed as special examiners to the American Board of Radiology and this is, I believe, the only one of the medical specialty boards which has physicists examine its medical and physical candidates in the physics pertaining to their specialty.

With the introduction of radioactive isotopes to the medical field, some of the old problems of radiologic physics became once more acute, and innumerable new ones were added. Those physicists who had long been engaged in work on radiologic problems connected with the medical use of roentgen rays and radium have devoted themselves to the study of the new agents, especially on questions pertaining to dosage and protection. In addition, a large number of younger physicists who have grown up with the atomic energy projects have entered the field of "hospital physics" as the British aptly call it. It is to these "hospital physicists" that the medical radiologists come most frequently for information and advice concerning the special problems presented by the addition of isotopes as sources of therapeutic radiations.

Radiologists know that the basic principles in the use and measurement of ionizing radiations are essentially the same, regardless of their sources.[8] The fundamental procedures developed during a half century of use of roentgen rays and radium, such as measurement of ionization in air, plotting of absorption curves of different radiation beams, evaluation of permissible dose and other dosage quantities, are directly applicable in the use of isotopes, although the technique and instrumentation involved has had to be altered and has become considerably more intricate and elaborate.[16]

But despite previous knowledge and numerous new publications available on isotopes and the details of their medical use, the actual and practical steps involved in inaugurating this type of treatment still present a confusing and formidable problem to individuals and institutions who have not been associated with any of the Atomic Energy Commission research projects. I belong to that group and my own experience furnishes excellent testimony of this fact; after having labored over some of the basic principles I almost daily receive personal inquiries and written pleas for further information from well trained radiologists who are utterly bewildered by the procedures involved in the procurement and use of radioactive isotopes.

These professional specialists are definitely awed when they read or hear others refer glibly to Circulars D-4 and A-3 or E-22, or about AEC-374. They are uncertain about what might be involved in signing three copies of a "Certificate of Compliance with Federal Food, Drug and Cosmetic Act." They also are decidedly bewildered by the host of advertisements and descriptions of the multitude of Geiger tubes and scalers, rate meters and crystal counters. They are nonplussed to hear that the ionization chamber which they are accustomed to using seems to have become "old-fashioned" and frequently is frowned upon for isotope work. In fact, to many radiologists it seems that all they have learned about radiation dosimetry and protection measures has become hopelessly outdated and inadequate to cope with these new and seemingly unlimited atomic energies. This feeling of inadequacy is present to an even greater degree in those physicians, not previously trained in radiology, who become interested in use of radioactive isotopes for special medical problems.

In view of the facts just cited, I shall try to outline the actual steps to be taken in the establishment of an isotope department, with emphasis on the practical problems involved, according to our own experience in the establishment of a functioning department at the Cleveland Clinic. In doing this, I shall undoubtedly repeat a good deal that has been published on this problem by others, for numerous excellent articles and documents on the subject are available. Among these are the many documents on the various phases of work with isotopes in medicine, on handling of radioactive isotopes, on radiation protection and instrumentation and the disposal of radioactive wastes that have been issued by the Isotopes Division of the Atomic Energy Commission in Oak Ridge.[17] The highlights of these recommendations have been interpreted by other scientists,[11,15]

probably most ably at the meeting of this Society last year, by Edith Quimby and C. B. Braestrup,[15] in a paper, "Planning the Radioisotope Program in the Hospital" which meanwhile has been published in the January, 1950, issue of this Journal. Braestrup has also discussed protection problems relating to isotopes in Portmann's "Clinical Therapeutic Radiology."[9] The second volume of "Medical Physics"[8] contains material on protection and health physics by K. Z. Morgan and on toxicity of isotopes by Brues. The measurement of radiation from isotopes is covered by Evans. Special problems relating to the medical use of isotopes are discussed by Hahn, Low-Beer, Miller, Gibson, and Aebersold.

The practical problems that have to be met and solved in the establishment of a department for work with radioactive isotopes may be subdivided into the following headings: (1) the formation of an isotope committee, (2) the procurement of proper equipment, (3) the procurement of radioactive isotopes from the Atomic Energy Commission, (4) storage and handling of these materials, (5) protection of personnel, (6) standardization of dosage, (7) disposal of radioactive wastes and, finally (8) the meeting of new problems as to equipment and personnel created by expanding functions of the department.

The Formation of an Isotope Committee. In institutional work, the first step in meeting any new situation is the formation of a committee to deal with it. The Atomic Energy Commission has set up criteria for the formation of a committee on isotopes in a hospital, which are readily available in the documents previously mentioned. An elucidation of these criteria is furnished by our own experience.

Since the treatment of thyroid diseases has always been an important function of our own institution, we naturally followed with keen interest the progress in the use of radioactive iodine, ever since the pioneer work of Soley, Hertz and Hamilton about ten years ago. However, it was not until 1947 when isotopes became generally available from the nuclear reactor at Oak Ridge that one of our surgeons specializing in thyroid surgery and our endocrinologist decided to use radioactive iodine in tracer studies and in treatment. It was at their suggestion that an Isotope Committee was formed. In addition to the physician and surgeon just mentioned, this committee included the medical director of research, the therapeutic radiologist and myself as radiation physicist, although at that time I could devote only part time to the work. The therapeutic radiologist was promptly elevated to the chairmanship of the committee, after the preliminary discussions had revealed that he was the logical person to perform this function. At the time this action seemed to go beyond the recommendations of the Atomic Energy Commission which suggests that a therapeutic radiologist be only a member of the isotope committee or even be available only as a consultant.

Our experience during several years has definitely demonstrated that the therapeutic radiologist should be the chairman of the isotope committee and that he, always working in the closest cooperation with the radiation physicist as sub-chairman, should supervise the ordering, handling and disposal of isotopes, calculation of dosage, the devising of protective measures and the actual application of isotopes in research, diagnosis and treatment.

Although this would seem to be the ideal arrangement, since the radiologist or radium therapist already possesses a thorough training and experience in the various aspects of medical use of ionizing radiations, I realize that this solution is not always possible. In the first place, there are still relatively few physicians who devote their entire time to therapeutic radiology. The director of a combined radiology department including both diagnosis and therapy often is too busy to take on the new and heavy responsibility of an isotope department, or he may be insufficiently interested in the therapeutic application

of radiation. In some instances, he may even be reluctant to add the new and dangerous tool to his already cumbersome armamentarium.

The human factors of prestige and local custom or habit may also present difficulties in the selection of the person or persons to handle the problems of isotope treatment. Throughout the country there is considerable variation in the personnel engaged in this work. I have seen splendid departments for isotope therapy at large institutions under the direction of various medical and non-medical specialists who do not confer with their fellow radiologists about dosage calculations or protective measures. I have visited institutions in which the radiologist and in some instances even the physicist closely guard their monopoly of the medical use of isotopes without consultation with their colleagues from other medical specialties. If this situation at first seems somewhat incongruous, it must also be remembered that for many years radium treatments have been given by surgeons and gynecologists without consulting the radiologists, simply because in the early days of radium therapy the surgeons were more prompt in acquiring the rudiments of radium application than the radiologists were to learn about radium surgery. Only recently, since radium treatment techniques have been more carefully worked out, and hence have become more complicated, has the radiologist slowly come back to his logical position in the sphere of radium therapy, working in close cooperation with the surgeon. Should history repeat itself and leave the medical use of radioactive isotopes in the hands of non-radiologists, it may take another generation or longer before the radiologist securely includes isotopes in his armamentarium. If that should happen, the splendid suggestions by Douglas Quick[12] in his Carman Lecture in 1947 and of U. V. Portmann[10] made in his presidential address to the American Roentgen Ray Society in September, 1949, that a separate specialty of therapeutic radiology including the use of isotopes should be created in all the larger medical institutions, may meet serious obstacles.

The foregoing may be something of a digression, but I feel that it sheds a significant light on a complete understanding of the situation involving the various aspects of the use of radioactive isotopes. At the outset, it is not only worth while but important to strive for that collaboration which, in the final analysis, is imperative and requisite for successful therapy.

The suggestion that I would make, then, about the formation of a committee on isotope treatment is that it should consist of (1) a radiologist, preferably a therapeutic radiologist, (2) a radiation physicist, preferably a full time qualified physicist, (3) a physician trained in internal medicine and possibly specializing in hematology. If this is not feasible, a fourth member who is a hematologist should be on the committee. Naturally it is advisable to add other members to the committee, such as a radiation chemist or some other specialist or specialists as the work expands and conditions require. The members of the committee must belong to a scientific institution of proper standing, possessing adequate equipment and laboratory facilities for this type of work.

Procurement of Proper Equipment. The acquisition of proper equipment is the second step in the inauguration of a functioning isotope department. If the prospective user of isotopes tries to gain information by visiting various medical centers and commercial companies he may find in some places large buildings filled with lavish equipment but he will also find one-room laboratories in which equally good work is being done with a few pieces of well designed apparatus.

What, then, is adequate equipment? When we started our isotope department in October, 1947, we had one Cyclotron Specialties 8 Scaler with a most unsatisfactory cyclotron Specialties Geiger tube but an excellent Victoreen Geiger counter tube for study of radioactive samples, one

Herbach and Rademan portable Geiger counter, and two old portable, but cumbersome, Geiger counters of our own design. We soon replaced these counters with a Victoreen portable Geiger counter survey meter, which with a directional tube of our own design we have used for measurements of the uptake of radioactive iodine in patients as well as for personnel monitoring. In addition to the counters, we had available from the roentgen therapy department a Victoreen radiation meter and a condenser r-meter. From our radon plant, some special tools and instruments were at hand. The total cost of this equipment used in our new isotope department was about $2,000. The figure of $3,000 given by Quimby and Braestrup for instruments and auxiliary equipment is in line with this.

Allocation of space for the isotope department depends very much on local conditions. We were fortunate in that space was not at a premium and we could place our instruments for measurement of uptake or determination of specimen samples with minute quantities of radioactivity far away from the isotope storage space. If such an arrangement is not possible, a resourceful operator with proper protective materials can do wonders with even a small space.

In our own department, we were fortunate enough to inherit the old lead walls from a roentgen therapy department which had been dismantled. With a simple mold we have made a large supply of 2 by 4 by 6 inch lead bricks which are very useful in building up proper protective walls. Such lead bricks are now on the market, of course, but I mention our home-made ones to emphasize the point that sometimes much of the necessary material and equipment can be fashioned from materials at hand. Many other useful tools and gadgets can often be made in the hospital or assembled from material found in the stock and storage room. This applies to remote-control pipets, lead glass windows, long forceps for handling tubes with radioactive solutions, etc. This statement is not meant to minimize the value of the many fine instruments which are available, but to point out that where the financial resources are limited, it may be possible to curtail the expense of an isotope department considerably by creative use of discarded roentgen ray and radon plants and other laboratory equipment. I do not intend to stress here how important and wholesome this economical approach would be to the scientific attitude of many young atomic scientists, who, being surrounded by abundant laboratory equipment, will often miss the exhilarating feeling of having "created" some of the fundamental apparatus themselves.

Procurement of Radioactive Isotopes. After the local isotope committee has begun to function and the minimal requirements for adequate equipment and facilities have been fulfilled, the next step consists in obtaining the desired radioactive isotopes from Oak Ridge. This necessitates a definite routine which at first seems unnecessarily cumbersome, but which cannot be avoided in view of the hazards involved in using radioactive isotopes. The procedure has been described elsewhere,[15,17] so I will not repeat the details except to say briefly that an application for allocation of the isotopes desired has to be submitted to the Oak Ridge National Laboratory, Oak Ridge, Tennessee. From there it is referred for action to the Subcommittee on Human Applications of the Atomic Energy Commission. At the same time, a contract on terms and conditions for order and receipt of radioactive by-product materials must also be signed and forwarded to the Oak Ridge Laboratory. Once the application for allocation has been accepted by the Subcommittee on Human Application, the applicant fills out an authorization for isotope procurement and signs a certificate of compliance with Federal Food, Drug and Cosmetic Act. Both of these are forwarded with a purchase order for a given amount of a given isotope to the supplier in Oak Ridge or to one of the companies authorized to dispense these radioactive substances.*

* For example, the Abbott Laboratories in Chicago or Tracerlab in Boston.

In the beginning these procedures seem complex, but they quickly become a matter of mere routine. It has been our experience that the Oak Ridge authorities have been invariably courteous and helpful, not only in furnishing the isotopes requested, but also in supplying helpful literature and personal advice. Although we are a private institution and have no connection with the Atomic Energy Commission nor with any other government project furnishing subsidies of financial aid or equipment for studies with isotopes, we have to date received promptly upon order over sixty shipments of I^{131}, amounting to a total of 9,000 millicuries, for tracer studies and the treatment of thyroid diseases, including cancer. Numerous shipments of P^{32} for the treatment of polycythemia vera have been obtained from the Abbott Laboratories, whose scientific personnel has also been extremely helpful in furnishing us with I^{131} in corn oil for fat metabolism studies in animals and the human.

Storage and Handling of Radioactive Isotopes. On receipt of the isotopes, they must be transferred immediately to the protective storage space which has been prepared for them. The lead shipping container for gamma-ray emitting isotopes is then returned according to instructions. Beta-ray emitters are received in containers with only a thin lead protective covering which may be discarded.

Protection of Personnel. Measures for the protection of personnel involved in isotope work like all other measures of handling radioactive substances are based on common sense and knowledge of the amount and energy of the radiation, the half-life of the isotope and the permissible dose of 300 milliroentgens per working week which has been generally established in this country, to avoid health hazard, to those handling the material. Radiation physicists have worked out tables of the various properties of the commonly used isotopes and have devised simple formulas for calculation of distances and of thicknesses of various absorbers required to reduce undesired radiation to the permissible dose. So long as the amounts of isotopes handled in the new department are relatively small, that is, of the order of less than 100 millicuries per month, these rules are relatively simple to apply, provided the one using the material is careful and prevents contamination of rooms and equipment from spilling of radioactive solutions. Even so, continued vigilance with the help of monitoring survey meters must be maintained.

A very necessary supplement to these meters is furnished by the film badges which should be worn continuously by every person who comes into contact with any type of radiation. These register the total radiation, with rough differentiation as to its type, received by an individual each week. In the process of introducing these film badges to the personnel in the isotope department, we also started a three-month complete monitoring service with film badges for eighty-three persons who came in contact with any type of radiation in our institution. (Roentgen therapy, roentgen diagnosis, radon plant, medical and physical isotope departments, dental roentgen ray, ophthalmologic beta ray, nasopharyngeal treatments, dermatological department, etc.) This survey served a most useful purpose principally in education for proper protection, for it pointed out the few weak spots which were corrected, to the great satisfaction of the personnel involved. The results obtained by this general survey are of great benefit in the new isotope department which is continuously monitored with film badges.

As the isotope department grows—and according to our experience if it is properly administered, it inevitably will grow—additional steps for protection have to be undertaken. For a time, we were able to handle larger amounts of isotopes in our radon laboratory which has a satisfactory hood, stainless steel tables and other equipment designed for construction of special radon applicators and gold seeds. However, when the traffic in that department became too heavy to insure proper protection to everyone, it was decided to transfer the hot laboratory to a remote corner of the

roof of our old Clinic building, where it is far removed from traffic by staircase or elevator and has the advantage of ideal ventilating conditions. Once more, it should be noted that we have also profited by numerous helpful suggestions for the equipment of such hot laboratories by consulting published data readily accessible to everybody.

Standardization of Dosage. By the time everyone in the new department is satisfied that the newly received isotopes are safely stored and that all rules for safe handling by the personnel are being followed, then the question arises as to whether the amount of radioactive substance obtained has been accurately calibrated, as indicated on the slip which accompanies the shipment.

Today the operator of an isotope department may feel confident that the calibration accompanying each new shipment is reasonably correct and that the discrepancy between calibrations of the same amount of a radioactive isotope by different laboratories is slight. However, that was not the case until recently. The variation in calibrations obtained by different laboratories for the same sample used to exceed 100 per cent. The tremendous improvement in the accuracy of calibrated samples of radioactive isotopes has resulted from a most remarkable cooperation between the Atomic Energy Commission, the National Bureau of Standards and the various users of isotopes who are equipped to make their own calibration measurements.

When we obtained our first shipments of radioactive iodine, I was still occupied by a war project on hemorrhagic shock and hence could devote but a small part of my time to the calibration of new radioactive products. We accepted the Oak Ridge values furnished with the material as our standard but submitted every shipment to the procedure we had applied to our radon applicators for many years. That is, we measured the gamma-ray emission of every shipment of radioactive iodine from Oak Ridge under as closely identical experimental conditions as were possible. The result of these measurements made on over sixty shipments at two-week intervals from October, 1947, to date tells an interesting story. While the relative values for milliroentgens per hour for a millicurie of I^{131} under standard experimental conditions of distance and intermediate absorption during recent months have varied only a few per cent, this was not the case prior to July, 1949, at which time there was a sudden but pre-announced drop in this value of 75 per cent. Before this readjustment in 1949, fluctuations in the results were of the order of ± 25 per cent.

Since this situation has been most satisfactorily corrected, it may seem irrelevant to mention it in connection with the establishment of a new department for isotope therapy. I have mentioned this circumstance, however, to show that it teaches an important lesson, and that is, do not underestimate the difficulties in dealing with a new physical agent!

The Atomic Energy Commission was well aware of these difficulties, and in November, 1948, dispatched an expert to help laboratories dealing with isotopes to arrive at more nearly uniform values in their standardizations of the most widely used isotopes such as I^{131} and P^{32}, especially in regard to their beta-ray emissions. His assistance—and I am one of his most grateful pupils—in proper measurement of the absorption rate of emissions from radioactive isotopes in aluminum, as compared with properly calibrated Ra D+E standards prepared by the National Bureau of Standards, has eliminated most of the previously existing difficulties. Calibrated samples of I^{131} and P^{32} sent to individual laboratories for comparison in recent months have further contributed to more uniform standardization of these isotopes throughout the country. In our own case, for example, we found that the last sample of P^{32} sent to us by the National Bureau of Standards in February, 1950, agreed with our P^{32} standard well within the experimental error. All values for our clinical

shipments of P^{32} from the Abbott Laboratories again well agree with our standard within the same range.

Hence, at the present time, the new isotope laboratory may safely rely upon the value furnished with radioactive material by the supplier. However, in an active department, the radiation physicist will soon desire to check on these values himself. A calibrated Bureau of Standards Radium D+E standard or any similar commerical standard with instructions, a set of calibrated aluminum filters, a good Geiger counter apparatus and a most careful pipeting technique will permit him to do so without much difficulty.

When there is no doubt about the proper strength of the isotope, the radiologist then wants to use it, for example, in tracer studies on the uptake of iodine in the thyroid gland. He wishes to know more about the dose necessary for that test. Here again, the radiologist starting today may profit by the experience of those who have already faced this problem, for a good Geiger counter permits him to make a satisfactory test with a tracer dose of as small as 50 microcuries of I^{131}. Our own tracer doses now have diminished to the level of 50 microcuries, but they were approximately ten times as large when we began our work. Our early more or less homemade instruments did not permit satisfactory detection of smaller amounts of radioactive substance. Promptly, however, we improved our instrumentarium so that the tracer dose could be reduced to about 0.3 millicurie. Recently we made the further reduction to 0.05 millicurie, or 50 microcuries, a dose that any newcomer with proper equipment will start with. The use of scintillation counters, which have recently appeared in this ever-changing isotope picture may permit further reductions of tracer doses.

Another lesson learned in our early work with I^{131} was inherent in the attempt to evaluate the uptake of the iodine in the gland. We had many patients from out of town, and since hospital beds were then unavailable for them, our checks on uptake had to be made within a few hours after ingestion of the I^{131}. Today, we feel that such checks on uptake with Geiger counter measurements are of limited value, although some investigators believe that twenty-four hour tests, when the uptake usually is at its maximum, are useful. At present, we use the twenty-four hour check whenever it is feasible. Even these, however, should be supplemented by studies of excretion rate of the applied iodine in the urine. However, excretion tests, unless these are most rigidly controlled, yield information which is often difficult to evaluate, and for this reason, some prominent investigators have even abandoned them. We are now investigating the conversion test devised by Dr. Dwight Clark at the Billings Hospital in Chicago. In this test, after injection of about 1 millicurie, the rate of conversion of orally administered radioactive iodine into the protein-bound iodine of the plasma is studied.

In cases in which treatment with radioactive iodine is indicated the tracer dose will be followed by a therapeutic dose. The radiologist is confronted with the task of calculating the proper dose of I^{131} to accomplish the desired purpose. This is a special study in itself, to the clarification of which Quimby, Marinelli, and others have made great contributions. Since it is a problem also involving clinical considerations, I shall refrain here from repeating what others have said more authoritatively than I can say it, and shall refer you to their publications for general information as to the dosage of radiation delivered by radioactive isotopes.

Disposal of Radioactive Wastes. The final step to be considered in the establishment of an isotope department is the arrangement for proper disposal of radioactive waste products. Definite suggestions for the handling of this problem have been made by the Isotopes Division of the Atomic Energy Commission, and interpretations of these suggestions for the hospital using isotopes have been incorporated in several textbooks. Common sense would dictate

the disposal of such substances directly into the main sewer or the incinerator provided the amount of radioactive material is not excessive and is properly diluted.

Problems of an Expanding Department. In retrospect, our experience and also the experience of many others show that the requirements for inaugurating a satisfactory department for the use of isotopes at a medical institution are not difficult to fulfill, although they may have appeared bewildering and somewhat formidable at the outset. Once the work of the department is actually in process, all the obstacles that seemed so cumbersome and even insurmountable in the beginning become every-day routine, and as stated previously, the department expands rapidly. With such growth, there comes the need for replacement of apparatus to take care of increasing volume, supplementary equipment and accessories for special uses and the addition of instruments, personnel and laboratory space.

For example, if, as happened frequently to us, the demand for measurements of radioactive samples of excreted urine of patients receiving I^{131} reaches great proportions; if, in addition, tests on conversion rates of iodine are added, and if the iodine in fat metabolism is being studied by analysis of blood samples from animals and humans then the life of the sample-counter technician begins to become a nightmare. When that point of activity is reached, it becomes expedient to replace the equipment for sample counting on a small scale with completely automatic counting equipment. We were faced with the necessity of acquiring such an apparatus to save the work of an extra technician. This required an additional expenditure of about $2,200 but saved the salary of a technician.

As another example, if work with low energy beta rays, such as those emitted by C^{14} is planned, a special low energy beta-ray counting apparatus must be added, at a cost of about $1,000.

However, if the isotope laboratory has reached the stage of function in the hospital which indicates the need for such additional apparatus, it is obvious that sufficient experience has been gained by the personnel to enable them to trust their own judgment, and they will be capable of constructing or selecting equipment for future needs without outside advice.

The foregoing outline of the basic requirements and the practical steps to be followed in the establishment of an isotopes department makes very clear the need for personnel well trained both in radiology and in radiation physics to help in the solution of the problems involved and in avoidance of undue health hazards from these new sources of ionizing radiations. Previously I spoke about the successful interplay between radiology and radiological physics. Would it not be highly desirable that this interplay should extend to both the physical radiologist and the radiological physicist?

Because in the future development of radiologic physics as applied to isotopes, the combined medical and physical approach is essential to insure that the proper use of all types of radiation will be guided into safe channels. Unfortunately, at present there are only a few medical radiologists who are also physicists. And among the many radiation physicists there are equally few who are real "hospital physicists." That is to say many nuclear physicists have not acquired their training by direct observation at the hospital bedside or in the cancer clinic in close cooperation with the therapeutic radiologist, the surgeon and the hematologist. I know that many of the younger physicists who come from atomic projects with an excellent training in physics are lacking in an understanding of the clinical approach and find great difficulty in acquiring a satisfactory attitude toward such work. There are even some who feel that for them hospital training is unnecessary and resent any effort that would modify their purely physical attitude.

As one small example of this one-sided attitude, I might mention an incident in

my own experience. I explained to a brilliant young nuclear physicist working in a government hospital the desire of one of our surgeons for a small probe-like directional Geiger tube for locating differential accumulations of radioactive iodine in thyroid tissues. Without any further consideration of the particular problem this physicist answered: "Such a tube is of no practical use for that purpose and we would tell our surgeon so." Such a non-compromising attitude in problems of medical physics will make proper progress more difficult and may alienate surgeons and physicians who are in need of information and whose collaboration in working out practical problems in the clinical use of radiations may be of great value for the progress of radiology.

It is therefore my firm opinion that the manifold uses of radioactive isotopes for medical purposes as well as the health control of all those who work with these substances should be guided, controlled and managed by the Department of Radiology. I believe this for two important reasons: (1) Over-all control of radioactive materials will be in the hands of those who have had experience for many years in the handling of dangerous radiations. (2) It will encourage the addition of properly trained physicists to the departments of radiology throughout the country. The radiation physicist, working in close cooperation with the radiologist, will also be available to any member of the medical staff for consultation on any problem involving radiation, and on other problems in medical physics.

Today this ideal is still far from fulfillment. And this is to be deplored and corrected as rapidly as possible. As a matter of fact, physicists working with medical men other than radiologists may give the medical collaborator a false sense of security because he feels that the physicist naturally knows all about radiation dosage and health hazards. The physicist, in turn, is often under the impression that the assistance he is receiving from the medical man on clinical application of isotopes is adequate and comprehensive. Actually, in such a combination, neither the medical man nor the physicist may be competent to solve the problems presented, since neither one has had any real experience in observing or evaluating the effects of irradiation.

To correct this situation, thorough training of radiation physicists in the environment of the clinic and the hospital by teacher physicists who have collaborated with medical men for years in the solution of radiation problems is highly desirable. Universities and private institutions equipped to furnish this training must in the future train a far greater number of biophysicists than at present. Departments of biophysics must be established at all schools which now have no such training to offer. There is no doubt in my mind that at present there are far too few hospital physicists available to fill the general need. Furthermore, the requirements for obtaining the diploma in radiological physics from the American Board of Radiology should be made even more strict. It would seem to me essential that the diplomate in radiological physics should have a Ph.D. in physics or biological physics and that in addition he should have general practical experience in the radiology department and in other departments interested in medical physics of a hospital for at least three years.

Some of these requirements may seem too exacting, but I feel sure that Dr. Henry Harrington Janeway would support them. He found time, despite his busy clinical practice, to go to night school at Columbia University to study physics so that he could understand the application of radium more satisfactorily and safely in his surgical work. In addition, he persuaded a physicist to help him in the further solution of these clinical problems. I strongly believe that if he were with us today he would want to learn in the same eager way about the safe clinical applications of radioactive isotopes.

So, permit me, in conclusion, to express my sincerest thanks to the American Radi-

um Society for the invitation to add another chapter to the book of lectures which honors Dr. Janeway, one of the great pioneers in the therapeutic use of radioactive substances.

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TRAUMATIC CHYLOTHORAX

THE ROENTGEN ASPECTS OF THIS PROBLEM*

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LONG characterized as a structure situated in surgically forbidden territory, the thoracic duct now assumes a position of increased importance because of the many surgical procedures involving the contents of the posterior mediastinal spaces While the present report concerns a case of traumatic chylothorax resulting from an injury to the upper chest and neck, it also affords a means of surveying the advances in the surgical anatomy and physiology of this structure. Under the stimulus of the complex features associated with chylothorax, studies were undertaken to determine if additional significant aids in the solution of these problems could be found.

Traumatic chylothorax due to intrathoracic rupture of the thoracic duct and the escape of chyle into the pleural cavity occurs rarely. While chylothorax is rarely reported, trauma to the lymphatic channels in the neck is probably not uncommon. Many authors have contributed to this subject following the first reported case by Quincke[63] in 1875. Early descriptions of traumatic chylothorax have been ascribed to Bartolet[3] in 1633, to Longelot[50] in 1663, and to Diemerbroeck[22] in 1685. Loe[49] in 1946 was able to gather 62 cases of traumatic chylothorax from the literature. Lampson,[44] up to the period 1947, was able to collect a total of 18 additional cases since the collective review of 41 cases by Shackelford and Fisher[73] in 1938. Chylothorax in children has been reported in about 25 cases. The mortality reported by Shackelford and Fisher[73] in 1938 in their excellent statistical review was 47.5 per cent. In Lampson's[44] analysis of 58 cases, he reported a mortality of 45 per cent. Dorsey and Morris[23] reported that surgical intervention in cases of traumatic chylothorax by ligation of the thoracic duct below the tear or attempts to repair the breach in the cut have been accompanied by an abnormally high mortality rate. Recent reports of chylothorax resulting from surgical trauma during the Smithwick procedure for hypertension with successful repair of the duct have been noted. Conservative measures without operative intervention have resulted in a mortality of 50 per cent.

The case reported below was treated conservatively, although surgical intervention was seriously considered in the latter stages of the patient's hospitalization. Various roentgenological and anatomic studies were undertaken in the interim in order to cope with the surgical problems concerned with the thoracic duct should surgery become necessary. Non-intervention, however, in this case was rewarded by a satisfactory recovery.

ANATOMY

The thoracic duct is the main collecting trunk of the lymphatic system originating in the irregular sac-like dilatation, i.e. the cisterna chyli which is situated opposite the body of the second lumbar vertebra. It crosses upward along the spinal column and passes through the aortic hiatus of the diaphragm. It ascends through the diaphragmatic opening into the posterior mediastinum lying below the aorta and the azygos vein, maintaining the same relative position somewhat to the right of the midline. At the junction of the last cervical and first thoracic vertebrae, the duct veers to the left and enters the neck behind the carotid sheath rising over the apex of the left lung. Here, it curves downward to enter the subclavian vein near its junction with the internal jugular vein. The thoracic

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duct drains all of the lymphatics below the diaphragm and the deep lymphatics from the dorsal half of the chest wall. When the thoracic duct is joined by the left bronchomediastinal subclavian and jugular trunks, it drains the lymphatics from the remaining portion of the left half of the body above the diaphragm. The duct forms an arch rising 3 to 4 cm. above the clavicle and crosses anterior to the subclavian artery. It is situated anterior to the vertebral artery and vein and the thyrocervical trunk or its branches. Most commonly, the duct empties into the vascular system at the angle of the junction between the left subclavian and left internal jugular vein, i.e. the angulus venosus. The right thoracic duct, which normally ends in the right subclavian vein at its junction with the right internal jugular, drains the right side of the head and neck, the right extremity and the right side of the thorax, portions of the convex surface of the liver.

The lumen of the thoracic duct is 4 to 6 mm. wide and contains several valves; the valves at the termination of the duct prevent the reflux of the venous blood. The duct is constricted at intervals and often presents a varicose appearance. It should be stressed that the location of the duct in the neck is not constant and that there are numerous frequent anatomic variations. That these variations are important when it becomes necessary to search for the ruptured duct in the neck is self evident. Similarly, it is important to recognize that many variations of the course of the thoracic duct in the posterior mediastinum are also present.

At first, various procedures were considered in the attempts to visualize the lymphatic system. This was done to review and devise a simple method of (1) demonstrating the thoracic duct and its variations, distribution and anatomic relationships, (2) to determine whether roentgen visualization of the duct was possible and if this visualization would aid the surgeon. Intentional visualization of the deep lymphatics in humans has not been attempted. The previous cadaver studies have made no attempts to systematically evaluate the thoracic duct in any large series of cases.

Shdanow,[74] Menkes,[54] and other observers, utilized various contrast media such as 20 per cent collargol and thorotrast to visualize the superficial and deep lymphatics in experimental animals. Thorotrast has been used by various observers to visualize the lymphatic and reticuloendothelial system. In view of the dangers associated with the use of thorotrast, it is no longer reasonable to use this contrast medium. The requirements which must be fulfilled by any contrast medium which is introduced into the lymphatic system or blood stream are well known.

In order to study the thoracic duct, injections of opaque contrast material were completed in a group of autopsy specimens. This is now being done routinely in order to collect a large group of cases. The first attempts to make the injections from the cephalic portion of the duct were unsuccessful since the viscid injection material could not be made to flow caudad on account of the valves in this region. Moreover the type of termination of the duct could not be visualized by this means. It was shown that the most efficient way of visualizing the duct could be completed by the following method: The duct was exposed immediately above the diaphragmatic margins and an injection of warm contrast material was introduced. Less than 5 cc. were used in each case. The contrast material flowed freely caudad and cephalad from this point. In contrast, the inability to fill the duct from its cephalic portion suggested that the valves were more efficient in this region than in the caudal portion of the duct.

Subsequent studies were then made by mixing a carmine gelatin mass with 10 per cent sodium iodide. By this means, the subsequent dissections of the thoracic duct could be carried out after the gelatin had been permitted to cool and comparison with the roentgen studies could be made. Since the roentgen studies provided an

adequate and easier method of visualizing the thoracic duct, dissections were not carried out in most of the cases. The injection studies demonstrated several important features. The wide anatomic variations in the course of the duct are demonstrated in the accompanying illustrations (Fig. 1, 2*B*, 2*C*). Davis[18] has described nine types of thoracic duct ranging from the complete persistence of the bilateral symmetrical ducts (Fig. 1, 2*B*) to the persistence of one single trunk. Many variations of cross anastomoses were encountered. These anastomotic channels are of marked importance in the development of a collateral lymph circulation following injury or obstruction to the main duct. Attention should be called to the bifurcations of the duct at the various levels of the dorsal vertebral bodies and the subsequent junction of these divided ducts (Fig. 1, 2*B*). These are very

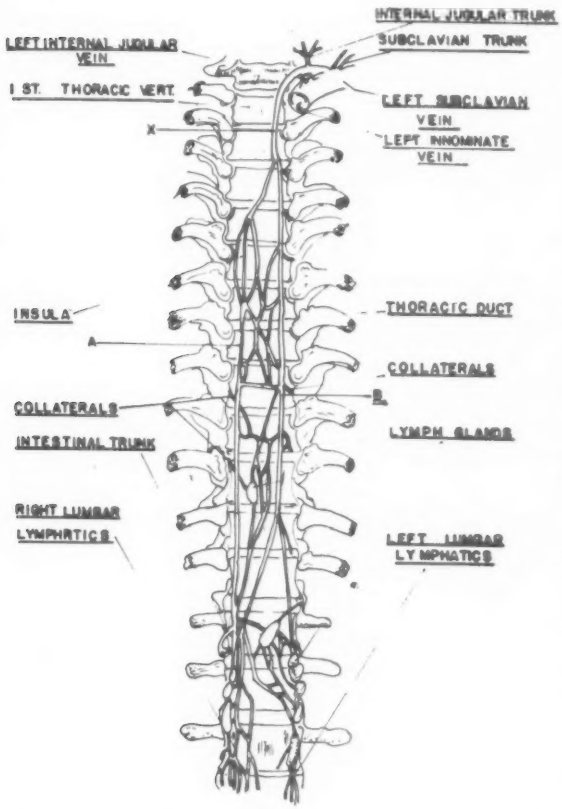

Fig. 1. Thoracic duct system in a white male, aged forty. This demonstrates a double duct. The thoracic duct begins in the abdominal cavity as two ducts and joins at the level of the lower third of the body of the second thoracic vertebra. The single trunk continues upward to open into the left subclavian vein a short distance from its junction with the internal jugular vein. No cisterna chyli was present. It was represented in this case by a plexus of lymphatic vessels.

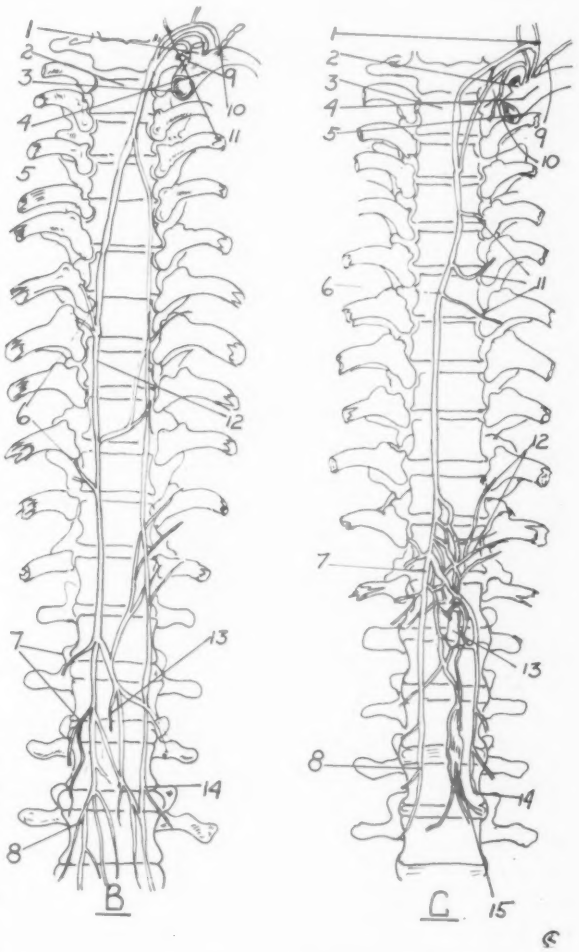

Fig. 2. (*B*) Thoracic duct system. Note the double duct and the reduction in size of the left duct. No cisterna chyli was present in this case. Multiple terminations into the venous system are present. Terminations into the left subclavian vein, the angulus venosus and into the left vertebral vein were present in this case.

(C) A thoracic duct in a female, aged sixty. Note the plexiform arrangement of the caudal portion of the duct and the cisterna chyli. There is an insula at its terminal portion. This duct arose in the abdominal cavity as a single trunk. Multiple terminations into the venous system were demonstrated in this case.

adequately demonstrated in the roentgenographic studies (Fig. 4*C*). Similar variations are also seen in the cervical area. These bifurcations were termed insulae by Haller.[35] The bifurcation and the associated anastomosing collaterals in this case probably represent the incomplete left thoracic duct. At no time was it possible to visualize the collateral lymph channels which drained from the intercostal spaces by means of the retrograde injection of the thoracic duct using lipiodol. Similarly, whenever the larger lymphatics drained in a caudal direction, filling of these channels could not be accomplished. Occasional filling of these channels by means of a more fluid contrast material, i.e. diodrast, could be accomplished. Additional studies of these channels using diodrast have been undertaken and these will be reported in greater detail elsewhere.

The mode of termination of the thoracic duct varied greatly. Although single terminations, i.e. single trunk, were noted in 75 per cent of the cases, multiple terminations, i.e. double, triple, quadruple trunks were also noted (Fig. 1, 2*B*, 2*C*). The injection studies also showed that while the duct may terminate in the left subclavian and in the left angulus venosus, in most cases it may also empty into the left innominate, the left internal jugular and into the left vertebral vein. In this group of cases, no duct was found to empty into the right internal jugular although such termination has been recorded by Davis,[18] and others.

Several observations could be noted during the injection experiments. The duct was able to distend from two to three times its normal caliber under the pressure of the contrast material. When a section of the duct was ligated and the proximal portion of the duct distended with contrast material, a large pressure was necessary in order to produce rupture of the duct. The numerous prevertebral and paravertebral lymphatic collaterals which joined the main thoracic duct served a very useful purpose in that these channels could be injected with methylene blue. Once outlined by this dye, the collaterals could be dissected until junction with the thoracic duct was reached. A similar method for locating the duct during surgical repair

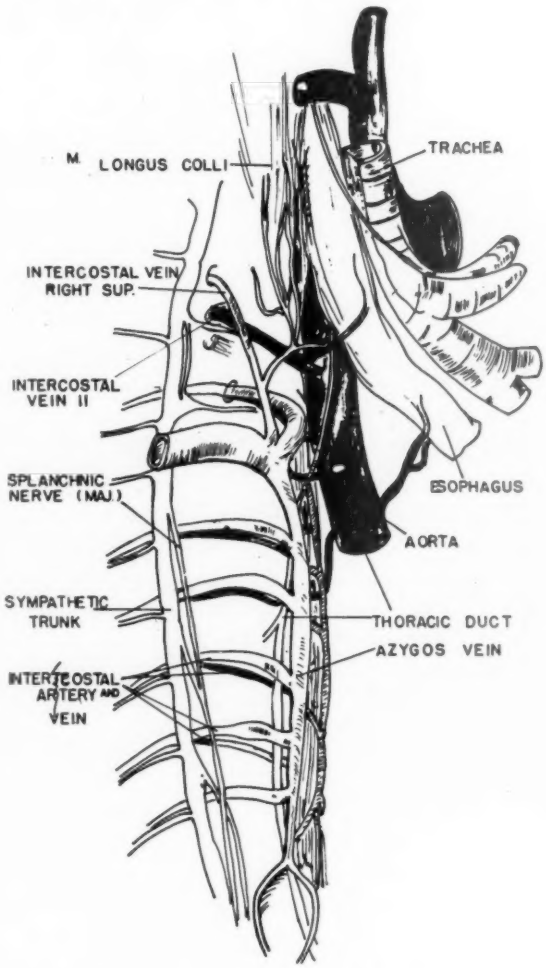

FIG. 3. The thoracic duct and the related structures in the thoracic area. An oblique view from the frontal and right. The aorta has been removed except in the tracheobronchial area. The arch of the azygos vein has been trans-sected and the vein turned laterally. The esophagus and the right bronchus have been pulled forward.

may be utilized. The studies showed that fewer valves are present in the lower portion of the thoracic duct than in its upper section. In many cases, no mid-dorsal or lumbar valves could be demonstrated.

For a long time, it was thought that ligature of the thoracic duct at its site of entry into the venous circulation would

produce complete obstruction resulting in death. Numerous investigators, however, demonstrated an extensive collateral circulation following ligature of the thoracic duct. Lee,[45] following the production of complete intrathoracic ligation of the thoracic duct in experimental animals, demonstrated by the subsequent anatomic studies of the animals that two general types of collateral circulation occur. This investigator demonstrated lymphatic connections in the abdomen with the lumbar veins. Lymphatic connections with the venous channels in other abdominal veins such as the renal and mesenteric veins have also been reported. Following ligature of the thoracic duct, the chyle may enter the circulation through a right thoracic duct or by means of anastomosing channels with the azygos or intercostal veins. Evidently, the primitive ducts are phylogenetically paired right and left channels. While the thoracic duct remains as the main channel, many of the cross communications are inactive and become atrophied. These embryonal lymphatic channels evidently play some part in the formation of a collateral which may develop following ligation of the thoracic duct. In 1937, Blalock *et al.*[7] attempted numerous operative techniques to produce complete blockage of the thoracic duct but were successful in a small group. On the other hand, ligation of the superior vena cava, with the resulting increase of the venous pressure, produced chylothorax in approximately 50 per cent of the experimental animals. Most investigators are now convinced that ligation of the thoracic duct in itself is not a dangerous procedure. It is evident that the lymphatic system contains an outstanding capacity for the development of a collateral circulation in most cases.

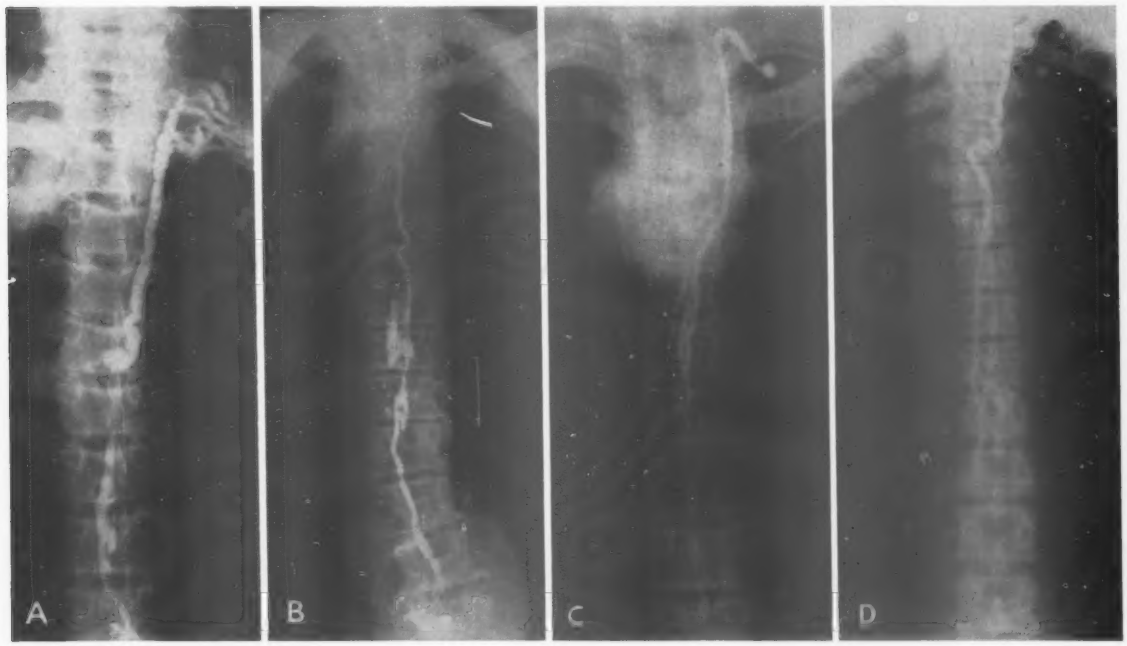

Fig. 4. Thoracic duct systems as demonstrated by means of injection of contrast media in cadavers.

The physiology of the thoracic duct has been adequately investigated and reviewed by numerous authors. More recently, Co Tui and his associates[15] have demonstrated that the lymph system is an important pathway in the physiology of the return proteins from the capillary filtrates to the blood. This system also acts in the mobilization of proteins from the depots in the body and is an extremely important factor in maintaining the blood volume and pro-

teins following hemorrhage. Forbes[31] has indicated in his recent report that the fat soluble vitamins A and D are lost in appreciable quantities in the escaping chyle. Approximately 60 to 70 per cent of the fat and the products of fat digestion from the lacteals of the intestinal villi are transported by this means into the venous system. The demonstration that fat transport from the blood stream to the thoracic duct does occur was shown by Reinhardt, Fishler and Chaikoff,[64] who utilized radiophospholipids injected into the blood stream. These investigators were able to recover 9 to 20 per cent of the lipids from the thoracic duct. When the hepatic production of lymph exceeds that of the intestine, the chyle of the thoracic duct is high in protein content. When it is realized that the lymph flow may range from 60 to 190 cc. per hour in the thoracic duct, any disruption in the continuity in this important channel will produce a serious alteration in the normal physiology. While the thoracic duct pressures are influenced by such factors as intraperitoneal and intrathoracic pressures, inflammations and food, the pressures in the thoracic duct may vary greatly. Pressure in the thoracic duct is usually higher than the venous pressures, which provide easy entry of the lymph into the veins at the base of the neck. The pressure in the venous junction into which the thoracic duct drains may be less than atmospheric pressure or zero. Following ligature of the duct, high pressures in the thoracic duct may develop, but these soon fall following the development of a collateral circulation. It has been previously noted that chylothorax may also be produced in approximately 50 per cent of animals in which the superior vena cava was ligated. This accumulation of chyle is evidently due to interference of the normal emptying of the lymphatic ducts into the tributaries of this vein resulting from the high venous pressure. As Blalock[7] points out, after a period of time the reaccumulation of chyle ceased, evidently due to the decline in venous pressure resulting from an increase in the collateral venous circulation. From this, it must be suspected that trauma to the venous channels in the neck may also play an important role in the production of chylothorax.

A variety of injuries may directly or indirectly produce chylothorax because of disruption or tearing of the thoracic duct. Macnab and Scarlett[51] have adequately outlined the causes of chylothorax. Shackelford and Fisher,[73] reviewing 41 cases with chylothorax, summarized the causes in the order of frequency as follows: crushing injuries, wounds by bullets or by stabbing, a fall from a height, blow on the chest, injury of the chest against the front seat of an automobile or sudden hyperextension. The position of the thoracic duct situated slightly to the right of the midline is considered an important factor in the accumulation of fluid on the right side. Chylothorax on the right is encountered most frequently, the site of the break in the thoracic duct being noted just above the diaphragm. It is also usually noted following indirect injury. Bilateral chylothorax associated with chylous ascites has been reported less frequently. Chylothorax on the left is caused by injury high in the course of the duct near its venous terminus. In approximately one-third of the reported cases, chylothorax followed trauma. It has also been suggested that a thoracic duct distended following a full meal is more apt to be torn or ruptured by trauma. In the remaining group of cases, the escape of chyle from the thoracic duct followed nontraumatic causes, most often associated malignant neoplasms involving the thoracic duct or the large veins. Lymphatic obstruction by filarial parasites is well known. Obstruction of the thoracic duct by tuberculous nodes and scarring caused by healed tuberculous lesions in the neck, the lungs, and mediastinum, has been considered a factor in many cases.

The position of the thoracic duct should be constantly considered during the course of extensive operative procedures in the chest. Injury to the thoracic duct during the

Smithwick procedure for hypertension is being reported more frequently in the literature. Intrathoracic operative procedures, such as lobectomy, esophagectomy, and gastric resections through intrathoracic approaches, require a constant vigilance to prevent injury to the thoracic duct. That operations on the left side of the lower part of the neck frequently endanger the thoracic duct is also well recognized. Neoplastic growths involve the duct in many instances and attempted removal of necessity exposes the duct to danger. Injury to the thoracic duct during the completion of a radical node dissection of aberrant thyroid carcinoma and during removal of a deep neck vein for biopsy has been reported by Loe.[49] Trauma to the thoracic duct during the cutting of the anterior scalenus muscle has also been reported by the same author. Brescia[9] has shown that the spontaneous types of chylothorax occur primarily in infants under one year of age. It should be kept in mind that rupture of the duct in infants may also be produced by hyperextension of the spine or vigorous attempts at resuscitation.

Leakage of chyle produces clinical reactions of two general types: symptoms which are due to pressure and those associated with the continuous external loss of lymph chyle. If the injury to the duct occurs in the chest, pressure symptoms resulting in various degrees of dyspnea soon ensue. The immediate reactions are of mechanical origin resulting from rapid accumulation of fluid in the pleural cavity. As the fluid accumulates, dyspnea becomes more severe. Most authors stress the latent period from the time of injury to the occurrence of pressure symptoms. The latent period is reported by various authors to range from a few hours to a period of several weeks. The delay in the appearance of symptoms is thought to be due to the extrapleural location of the thoracic duct or to secondary necrosis. The fluid accumulates and is confined in the posterior mediastinum first, later breaking through into the pleural cavity. The escape of the fluid into the pleural cavity is sometimes ushered in by dyspnea, shock and circulatory collapse. In our case, pressure symptoms were noted soon following the injury. The dramatic relief of symptoms following thoracentesis is unusually striking. The rapid reaccumulation of fluid may require frequent aspiration of the pleural space. Chylopericardium and chylous ascites may occur in association with chylothorax.

The continuous escape of large quantities of essential body fluids, rich in fat and in the same constituents as blood serum, produces progressive collapse, weakness, hunger and thirst. In a comparatively short period, emaciation and inanition, followed by general apathy, are noted. The pulse becomes weak and rapid and there is marked diminution in the urinary output.

With the rapid reaccumulation of chyle in the pleural cavity requiring frequent thoracenteses, dehydration and emaciation are more likely to occur. Because of the low serum proteins, peripheral edema may occur. In other cases where the chylous fluid reaccumulates slowly and infrequent thoracenteses are required, the patient may survive for weeks and even months. In the case reported by Blalock[7] of chylothorax and chylous ascites associated with a diffuse pre-existing thrombophlebitis, the patient lived for approximately sixteen months.

Chylous fluid obtained by thoracentesis is milky in appearance, containing finely emulsified fat globules. On standing, the the fluid shows three distinct strata: a creamy layer on top, a thinner milky layer below and, at the bottom, a layer of sediment containing cellular elements. While a concomitant hemothorax may render the chyle bloody in appearance, after repeated thoracenteses the color changes from red to a milky character and the correct diagnosis becomes apparent at once. The character of the fluid will vary with such factors as the fat and protein content of the diet and the degree of dilution by the pleural fluid. The oily nature can be established by the use of Sudan III stain. Extraction

of the fat by shaking the fluid with ether and determination of the fat content should also be done. Chyle is a filtrate and its constituents resemble those found in blood serum but in smaller amounts. The chylous fluid is alkaline in reaction with a specific gravity varying between 1.012 and 1.020. Odorless and sterile, the chyle resists putrefaction. Lampson[44] has demonstrated that chyle is bacteriostatic against cultures of *Escherichia coli* and *Staphylococcus aureus*. The fat count varies from 0.4 to 4 per cent with the diet of the patient, but is generally high. Although the protein content varies between 1 and 6 grams per cent, the total protein generally exceeds 3 grams per 100 cc. Following the onset of chylothorax or chyloperitoneum, the blood fats are reduced by approximately 25 per cent of their normal levels. The plasma proteins may fall steadily to such a degree within two to three weeks that levels as low as 3.8 gm. per cent may be reached. While the content of sugar, non-protein nitrogen, urea and amino acids are approximately the same as serum, the cholesterol and calcium contents are somewhat lower. Because of the relative excess of antithrombi and the poor content of thromboplastin, lymph clots slowly.* There is a considerable variation in the white blood cell count of chylous fluid which may range from 2,000 to 20,000 cells per cubic millimeter. While a few eosinophils, transitionals and unclassified cells may be found in the fluid, the lymphocytic cells predominate. A few red blood cells may also be found. Because of a loss of the lymphocytes with the continuous external loss of chyle, there is usually a drop in the lymphocytic count in the blood. This may be of diagnostic importance, together with the usual drop in the serum proteins and serum calcium.

Roentgenographically, the chylous fluid in the chest presents no features which differentiate it from other fluid densities. Although the chylous fluid contains fatty particles and lighter than blood or serous fluid, this cannot be differentiated by the present roentgen methods.

In view of the frequency of injuries to the thoracic duct following dorsolumbar sympathectomy, routine postoperative roentgenograms of the chest are indicated to determine whether a pleural effusion is present. Moreover, with the presence of a rapidly accumulating pleural effusion following such a procedure and a progressive falling lymphocytic count, trauma to the thoracic duct with chylothorax should be suspected.

Because of the position of the thoracic duct, it would appear that chyle escaping from a rent in the thoracic duct would collect in the posterior mediastinal pleural segments rather than in the costal segments Lateral and oblique projections, as well as frontal views of the chest, are necessary for accurate recognition in localization of fluid in such locations.

Thus, the small amount of fluid and pneumothorax are not satisfactorily shown in the first group of roentgenograms. Roentgenoscopy with visualization of the costophrenic sinuses during inspiration and expiration, followed by film studies in lateral recumbent position, did demonstrate a small amount of fluid. The use of the lateral recumbent position in film studies of the chest in order to cause gravitation of the fluid into the axillary region has been recommended by Rigler.[66] The marked increase in the amount of fluid between the first and the second studies which were made thirty minutes later is a unique feature. This was evidently due to rupture of the retropleural collection of the chyle and the perforation of the chyloma into the pleural cavity.

REPORT OF CASE

CASE 1. A white, six year old female child was brought to The Grace Unit Emergency Room one hour following injury. Her mother stated that while playing in the back-yard, the child had been pinned to the ground by a dis-

* The literature on the cellular composition of the lymph from the thoracic duct has been very adequately reviewed by Drinker and Field[24] and will not be repeated here.

carded piano sounding board, which had tipped over and fallen on the youngster. When extricated, the child was unconscious. Numerous abrasions of the left scalp, face, the neck and thorax were seen. The examining physician brought the child to the hospital immediately. When examined, the child had regained consciousness and, although well nourished, appeared pale and acutely ill. The respiratory distress of the child was striking and the patient complained of tenderness of the left chest and upper abdomen. Percussion and palpation could not be completed because of the extreme tenderness of the chest and abdomen. Auscultation

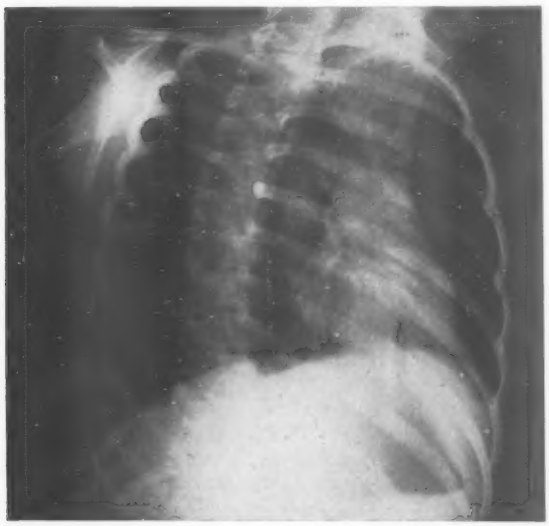

Fig. 5. Case 1. Oblique studies of the bony thorax for bone detail made in the upright position demonstrates no fluid in the pleural cavities.

revealed numerous rales and diminished breath sounds on the left. A marked expiratory grunt was noted. Because of the possibility of a ruptured viscus and spleen, roentgenographic studies were undertaken. The examination of the skull, bony thorax and dorsolumbar vertebrae demonstrated no evidence of fracture. The first film studies of the chest demonstrated mottled irregular densities overlying the left upper lung field. The roentgenographic studies of the chest at first demonstrated no evidence of pneumothorax on the left but a minimal effusion in the upper portion of the left pleural cavity was present (Fig. 5, 6). The effusion into the left pleural cavity could only be adequately recognized by fluoroscopy and by means of films made during marked expiration. The patient was placed in the left lateral decubitus position (Fig. 7) and twenty minutes later, reexamination of the chest was done and a marked increase of the effusion in the left pleural cavity was then noted, and films made in the upright position now demonstrated small

Fig. 6. Case 1. Approximately five minutes following Figure 5, a recumbent anteroposterior film was again made to exclude fractures of the ribs. The characteristic ribbon-like shadow extending from the diaphragm to the left apex along the periphery of the chest, indicative of pleural fluid, is shown in this film. Note the reduced translucency of the left lung in comparison to the right.

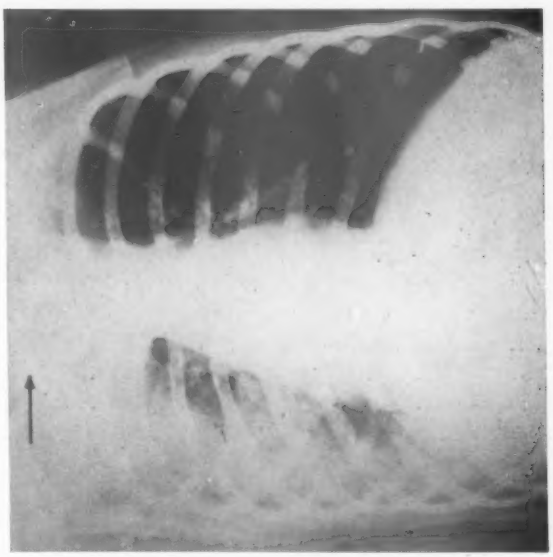

Fig. 7. Case 1. Lateral decubitus left side down. This film was made approximately twenty minutes following the first roentgenographic study. Note the marked increase of fluid since the first examination, i.e. Figures 5 and 6.

amounts of loculated air in the left pleural cavity.

The irregular mottling of the upper chest was thought to be due to edema of the soft tissues. Hemorrhage into the lung parenchyma was also thought to be present. A marked increase in the amount of fluid in the left pleural cavity was noted in the interim between the beginning and the completion of the roentgen examinations. A traumatic hemopneumothorax was considered to be present on the left side. Because of the rapid accumulation of fluid on the

FIG. 8. Case 1. Extensive left pleural effusion is demonstrated. This film was made prior to the first thoracentesis on March 23, 1948. Sixteen subsequent thoracenteses were done.

left side, other possibilities were considered; among them, traumatic chylothorax.

The patient was placed in an oxygen tent and given morphine grains 1/16. She vomited small amounts of clear fluid which were intermittently streaked with small amounts of blood. The chest examination the next morning revealed diminished breath sounds on the left side with dullness to percussion. The patient continued to improve and it was possible to discontinue the oxygen for long periods. The cyanosis which had been noted following her trauma was less noticeable. Her respirations remained rapid and shallow. Seven days following her admission, the first thoracentesis was performed. Approximately 850 cc. of cloudy sanguineous fluid was withdrawn and the patient was returned to the oxygen tent. The true nature of the fluid confirmed the diagnosis of injury to the thoracic duct. A second thoracentesis was repeated three days later and 1,550 cc. of milky fluid was withdrawn. Her respirations following the second thoracentesis became slower and although the child was moderately exhausted by the ordeal, her condition was much improved. The serial chest films demonstrated the reaccumulation of fluid (Fig. 8).

Although the patient was much improved following each thoracentesis, this was done only to relieve the dyspnea, since it was believed that the pressure of fluid would tend to limit the flow of chyle into the pleural cavity and in this way aid in the healing of the torn thoracic duct. The patient was given a diet high in protein contents and with a low fat content. Numerous blood transfusions were given. Laboratory data are presented in a composite chart (see Fig. 9). The amount of fluid withdrawn at first by thoracenteses varied from 1,850 to 2,350 cc. The patient continued to improve so that the time interval between the thoracenteses was gradually increased to approximately six days. Twenty thousand units of penicillin were instilled into the pleural cavity following removal of the chyle. After a lapse of six weeks, despite the improvement of the patient, surgical consultation with Dr. Gustav Lindskog was obtained to determine whether or not surgical intervention for closure of the duct was feasible. The patient, however, at this time showed a marked decrease in the amounts of fluid following thoracentesis so that in a period of one week, the fluid diminished from 800 cc. to 20 cc. Numerous laboratory studies were obtained throughout the entire admission. A total of seventeen thoracenteses were completed with the removal of 17,553 cc. of chyle. In spite of the high carbohydrate, high protein diet, her blood serum protein fell from 7 grams to 5.53 grams. The average protein concentration of the chyle was approximately 2.8 per cent and the average concentration of the lipids was approximately 2.4 per cent. Studies of the serum fatty acids showed the average of these to be approximately 13.6 mg. per cent. The total serum cholesterol was 159 mg. per cent. The average values of the chyle lipids from the chest fluid showed the fatty acids to be approximately 14.3 mg. per cent. The cholesterol contained in the chyle was 96 mg. per cent. The patient's weight on admission was 45 pounds. On April 29, 1948, when

transferred to the Thoracic Surgical Service of The New Haven Unit, her weight was 43½ pounds. On May 8, 1948, her weight was 40 pounds. When discharged, the patient weighed 42 pounds. While the white blood cell count fell from 19,800 on March 16 to 7,500 on April 30, 1948, no marked subsequent changes were noted thereafter. The studies of the lymphocytes and eosinophilic percentages are shown in Figure 9. Cultures of the chyle were made throughout the entire study and these showed no growth. Bacteriologic studies of the chyle were made throughout the entire period and these showed no growth.

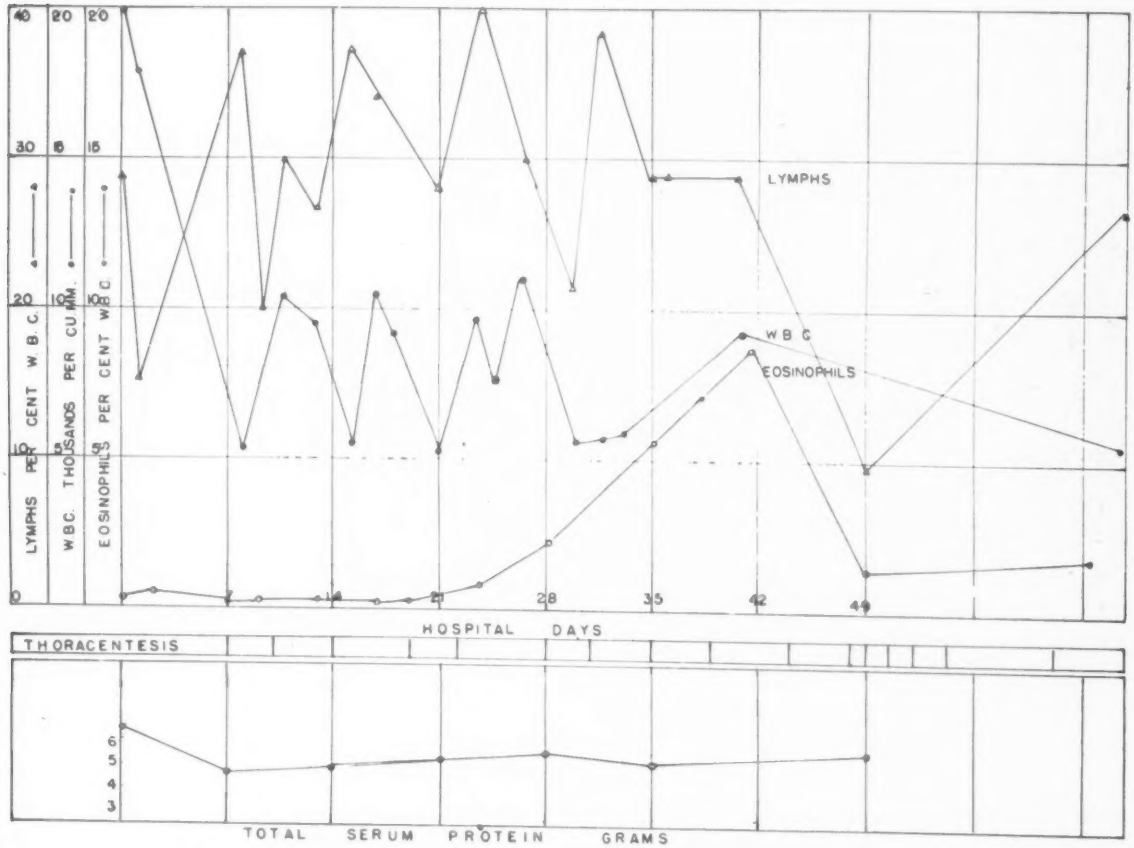

Fig. 9. Case 1. The composite chart above demonstrates the effects of chylothorax on the serum protein concentration and the number of circulating lymphocytes. The rise in eosinophils was thought to be due to a foreign body response. The maintenance of the lymphocytes in the blood despite the chylothorax seemed to indicate that a collateral channel or channels existed which enabled lymphocytes to enter into the circulating blood.

On the sixty-second day following her admission to the hospital, the patient was discharged. Approximately nine weeks following her hospital admission, she was re-examined and the roentgen studies of May 24, 1949, showed the lung fields to be within normal limits and the costophrenic sinuses were clear (Fig. 10). The swallowing function at this time demonstrated no abnormalities. The patient was seen in the clinic on October 1, 1948, and appears entirely well. She is being followed in the surgical clinic at The Grace Unit.

TREATMENT OF CHYLOTHORAX

Several rigid requirements must be satisfied in the treatment of chylothorax. These are the prevention of the loss of chyle, the maintenance of nutrition and the prevention of infection in the chest, with measures designed to aid healing of the duct. The recent publication by Olsen and Wilson[58] describing 9 cases of chylothorax treated

at the Mayo Clinic indicates that the condition is not as rare as is commonly supposed. Eight of these cases, however, were non-traumatic in origin. Under any circumstances, chylothorax is a formidable problem and requires all the ingenuity that the clinician can muster in order to combat the situation.

FIG. 10. Case 1. Chest film on May 24, 1948. The study demonstrates no evidence of effusion. The patient had been discharged from the hospital on May 18, 1948, and has remained free of symptoms. No reaccumulation of fluid in the pleural cavity has been noted.

The medical measures employed to maintain the nutrition of the body are replacements of the serum protein and fat lost in the chyle. The marked dehydration resulting from the tremendous loss of fluid must also be vigorously combated. The conservative supportive measures are necessary to maintain the patient's nutritional state until spontaneous closure of the duct has taken place or until operative repair can be carried out. A high protein, low fat diet has been advised. The use of the low fat diet to diminish the flow of chyle has been recommended by many, although the limitations of the fluid intake and dietary fat apparently do not markedly reduce the volume of chyle. The intravenous administration of fluid, whole blood and plasma and administration of amino acids should be adequately utilized. Because of the poor concentration of thromboplastin and the relative excess of antithrombin in the lymph, the use of vitamin K and rutin should be kept in mind. The reduction of the volume of chyle contained in the pleural cavity and the prevention of respiratory and vascular collapse associated with the increased intrapleural pressure are controlled by means of thoracenteses.

Autogenous intravenous transfusions of chyle in the hope of preventing peripheral edema have also been carried out. Others have utilized intrasternal administration of chyle. While the parenteral introduction of chyle first recommended by Oeken[57] has apparently been of benefit in some cases, it is accompanied by many hazards. Whitcomb and Scoville[83] and Peet and Campbell[60] reported sudden death following the intravenous administration of chyle which they attributed to anaphylactic shock. Material has been presented by Johnson and Freeman[42] indicating that a hemolytic agent exists in chyle which is not found in other lymph. Other investigators and their co-workers have noted phlebothromboses and the extension of pre-existing thrombophlebitis following the intravenous introduction of aspirated chyle. Most authors agree that the intravenous use of acacia of blood plasma is a safer method of maintaining or restoring the normal osmotic pressure in the blood.

In the treatment of cases of chylothorax secondary to malignant disease, especially in the cases of lymphoblastoma, radiation therapy is indicated. The prognosis of chylothorax of non-traumatic origin is generally poor, since most of these cases are associated with varying degrees of malignancy.

The surgical procedures utilized in the treatment of chylothorax, on the other hand, have also met with little or no success at all until recently. As late as 1945, it was noted that direct surgery to repair the thoracic duct was completely unsuccessful, resulting in a 100 per cent mortality.

More recently, Brown[11] has reported the successful drainage of an extrapleural collection of chyle preceding the formation of chylothorax. Baldridge and Lewis,[2] on the other hand, believe that so far as drainage of a retropleural chyloma is concerned, it would be more logical to attack the duct directly, since the surgical exposure would be the same. The open exploration of chylothorax due to intrathoracic injury offers a more difficult problem because of the deep situation of the duct. Because of the unusual position of the thoracic duct, early operation for the traumatized duct is usually not undertaken. In the later stages, the poor condition of the patient makes operation difficult.

Various authors have reported inadvertent section of the thoracic duct or a collateral lymph channel incidental to splanchnicectomy and sympathectomy. In the case reported by Crafoord,[16] the distal stump of the thoracic duct inadvertently sectioned during sympathectomy at the level of the eleventh rib was crushed and buried in the adjacent mediastinal tissue, without the subsequent development of any untoward clinical manifestations. Crafoord[16] observed an undamaged collateral lymph channel and he ascribed the satisfactory outcome in this case to the existing collateral channel in this region. In the case reported by Whitcomb and Scoville,[83] the severed duct was closed by silver clips at the level of the first lumbar vertebra. The subsequent chylothorax was thought to be due to erosion and necrosis of the duct by the silver clips. Death in this case ensued under conditions considered by the authors to be indicative of anaphylactic shock. Whether necrosis of the duct actually occurred or insufficient collateral lymphatic circulation existed in this case could not be determined. In the case reported by Ehrenhaft and Meyers,[26] inadvertent ligation and severance of the duct without untoward subsequent incidents were noted.

Smithwick,[76] with a most extensive experience with thoracolumbar sympathectomy, estimates that he has injured the thoracic duct 15 or 20 times. Chylothorax, however, developed in 1 case only. Because of the surgical experiences gained following inadvertent ligation and severance of the duct during thoracolumbar sympathectomy, Baldridge and Lewis[2] have advocated a similar surgical approach to the lower thoracic duct with ligation of the duct in this area. Successful ligation of a ruptured intrathoracic duct following strenuous coughing has been reported by Lampson.[44] In addition, this author cites an additional successful ligation by Meade[53] but does not report the details of the case.

More definite surgical measures have been advocated by others. Deansley,[19] in 1903, advocated implantation of the severed duct to a nearby vein and successfully implanted a cervical thoracic duct into the left internal jugular vein. In 1916, Harrison[37] anastomosed the divided cervical thoracic duct into the left external jugular vein. More recently, Hodge and Bridges[40] were able to implant the distal portion of a thoracic duct severed during the second stage of a transthoracic thoracolumbar sympathectomy into the azygos vein.

Under operative circumstances in which primary repair of the duct or venous implantation of the duct is impossible, simple ligation must be resorted to. This conforms to the opinions stated as early as 1907 by De Forest,[20] who noted that a wounded thoracic duct should be treated exactly as a bleeding blood vessel. Ehrenhaft and Meyers[26] have suggested suturing a muscle stump into place and applying pledgets of gelfoam impregnated with thrombin and plasm to the leaking stump. Smithwick[76] has occluded tears in the thoracic duct with fibrin foam soaked in thrombin solution. It should be pointed out that the use of sclerosing substances such as quinine hydrochloride have been utilized by Blalock[7] in order to produce occlusion of the duct in his experimental studies of the thoracic duct.

Attempts to produce closure of the ruptured thoracic duct by the introduction of foreign materials into the pleural space

has also been reported. It is difficult to understand how a thoracotomy or thoracoplasty would aid in the closure of a ruptured thoracic duct. Phrenicotomy of the affected side has been recommended by Nowak and Barton[56] in order to produce elevation of the diaphragm which would presumably close the perforation in the lower thoracic portion of the duct. It is questionable whether or not phrenicotomy would aid in the closure of the duct which has been ruptured in the upper posterior mediastinum. It is difficult to visualize how one would be able to determine whether the rupture has taken place in the lower portion of the thoracic duct near the diaphragm or in the upper posterior mediastinum.

DISCUSSION

While the outcome of the case presented above made surgical intervention unnecessary, the observations derived from this case, as well as the material compiled from the surveys, permit several comparisons. Much of the data reviewed concerns cases encountered following surgical trauma. That much of the knowledge gained in the treatment of chylothorax following surgical trauma may be applicable to cases of chylothorax associated with other types of trauma is evident. We believe that the many problems associated with chylothorax following surgical trauma are different from those associated with other types of trauma. For this reason, it is our impression that cases of chylothorax following surgical trauma should be kept in a special category.

In this group of cases, the cause and the approximate site of the trauma are known. It is of paramount importance that injury to the duct be kept in mind. If injury occurs immediate repair by one of the methods suggested by the various observers should be utilized in order to obviate the necessity of subsequent operative procedures. Moreover, it should be emphasized that failure to recognize surgical section of the thoracic duct has occurred in few cases. Just as there are many anatomic variations of the lymphatics, many variations of the anatomic position and the relationship of the splanchnic nerves are present. Poppen[61] has stressed that in the cases where the great splanchnic nerve enters the aortic hiatus, the relationship of these structures to the thoracic duct is close indeed. In the dissections which followed our injection studies, the splanchnic nerve was situated a few millimeters from the thoracic duct immediately over the azygos vein.

That injury to the thoracic duct is a hazard of major importance in the surgery of the posterior mediastinal contents is obvious. With the increased frequency of operative procedures in this area, it should be anticipated that the number of accidents of this type will increase. It may be surgically wise in such cases to identify and isolate the thoracic duct and its major collaterals before section of the splanchnic nerve is completed. The administration of a fat meal with or without Sudan III given several hours before operation will aid in distending the duct.

Subsequent roentgen studies should be done after all surgical procedures in which trauma to the thoracic duct may occur. In such cases, the roentgen demonstration of a rapidly accumulating pleural effusion associated with a low serum protein concentration and a falling lymphocytic count should be cause to suspect the presence of chylothorax. Moreover, the fluid contained from the thoracenteses in such cases should always be examined for chyle.

Chylothorax following external trauma presents problems which are somewhat different. While minimal trauma may cause chylothorax, trauma severe enough to cause rupture of the thoracic duct is usually of serious import. Following the preliminary treatment of shock, the surgeon is then confronted with the perplexing problem of treating the chylothorax. In these cases, the site of trauma is not known. Moreover, it should be remembered that surgical exposure of the thoracic duct is difficult and hazardous.

The usual course of such a case has been to treat the case conservatively, hoping for a spontaneous closure. When this does not occur within a reasonable time and there is a rapid accumulation of chylous fluid in the pleural spaces and emaciation and cachexia appear, the surgeon then turns to surgery. Ligation of the thoracic duct, utilizing the retropleural approach employed in the resection of splanchnic nerves, has been recommended for all types of chylothorax, regardless of etiology. Such a ligation would be adequate in all cases in which a single trunk thoracic duct is present. In such cases, ligation low in the thoracic duct would apparently prevent leakage high in the posterior mediastinal or cervical segments of the duct. In cases where persistent bilateral thoracic ducts are present, ligation of one system would not stop leakage of chyle in the other. Thus, in Figure 1 a rupture at site *X* would not be controlled by ligation at *A* or *B*. Adequate collateral circulation of the ductal system would maintain the pressure and leakage of chyle would continue. In such cases, it may be of value to visualize the ductal system at the time of surgery by means of contrast media such as are used to study the blood vessels and the urinary tract. Such studies may also aid in determining the site of the thoracic duct rupture.

In many ways, the results of the postmortem injection studies are disappointing, since an easy way of visualizing the thoracic duct in the human was not established. The studies, nevertheless, provide a stimulus for additional work in this field. The injection of the postmortem specimens were originally begun to provide an easy method of demonstrating the anatomy and variations of the thoracic duct roentgenographically. Because of the occasional visualization of the lumbar lymphatics by pyelolymphatic backflow, attempts to visualize these structures and the thoracic duct by retrograde pyelographic injection of the upper urinary tract under pressure were done. However, we consider this an unsatisfactory and, in some ways, a dangerous procedure. Moreover, the retrograde introduction of dye into the upper urinary tract under pressure does not produce pyelolymphatic backflow in many cases. The trauma which follows induced extravasation of dye into the kidney parenchyma, the venous and lymphatic systems, has produced very unfavorable sequelae.

The direct introduction of the contrast medium into the thoracic duct was then attempted in cadavers and autopsy specimens. This was achieved in two ways: (1) following neck dissection and exposure of the terminations in the left angulus venosus, and (2) exposure of the thoracic duct in the middle and lower dorsal areas, utilizing a surgical approach similar to that employed for lumbar sympathectomy. In the neck dissections, the terminations in the cadaver were found with moderate difficulty. Once the injection was made in the neck area, additional surgery to ligate the site of rupture in the thoracic area would be necessary in many cases. For this reason, this method was deemed unsatisfactory.

On the other hand, the retropleural approach to the thoracic duct provided ready access to the duct so that it could be injected as well as ligated at one and the same time. Moreover, the studies following surgical trauma to the thoracic duct indicate that ligation in this area will, in most cases, stop the chylothorax. Studies have been undertaken to determine whether or not dyes such as T-1824 or brilliant vital red which appear in the thoracic duct lymph shortly after intravenous injection will aid in visualization of the thoracic duct during operation.

In addition, we believe that hypoproteinemia may play a significant role in chylothorax. That proteins are essential to wound healing affecting the regeneration of tissue has not been adequately stressed previously. Various investigators have studied the effects of protein depletion on cellular repair, wound healing and vascularization of wounds. It is not unreasonable

to consider that hypoproteinemia plays an important role in the inability of the duct to healing satisfactorily.

The difficult and, in many cases, the insurmountable task of maintaining adequate serum protein concentrations has been encountered in nearly every case of chylothorax. Moreover, recent experimental work by Cain[12] has shown that intravenous introduction of fluids act as lymphogogues. Thus, attempts to sustain the protein level by intensive intravenous therapy would also maintain the pressure in the lymphatic system. This, in turn, would cause constant leakage at the site of the thoracic duct rupture since the pressure in the thoracic duct would also be constantly maintained.

With these factors in mind, in a patient who shows a continuously retrogressive course, with the demonstration of a rapid reaccumulation of the pleural fluid, conservative measures should be abandoned. In these cases, operation should be undertaken before the patient has reached a stage where major surgery is contraindicated as well as impossible.

SUMMARY

This paper is presented to emphasize the importance of the thoracic duct and to produce an awareness of this structure in the surgeon and radiologist. A case of injury of the thoracic duct following a crushing blow is presented. Satisfactory outcome of the case made surgical intervention unnecessary, although operation was seriously considered. Roentgenographic and anatomical studies were carried out in cadavers in order to demonstrate the thoracic duct and its relationships. An easy but adequate method of demonstrating the thoracic duct roentgenographically in cadavers and postmortem material is shown. The causes, symptoms and treatment of surgical as well as non-surgical chylothorax are reviewed and compared. Following operative procedures in which the likelihood of trauma to the thoracic duct is great, roentgen studies should be done in order to exclude chylothorax. A diagnostic triad is offered. In such cases, the roentgen demonstration of a rapidly accumulating pleural effusion, associated with a low serum protein concentration and a falling lymphocytic count, should be cause to suspect the presence of chylothorax. A program for additional studies in this field is stressed.

We are indebted to Dr. Morris Glazer for the use of this case. We are also indebted to Dr. Levin Waters of the Department of Pathology for his invaluable aid in the injection of the postmortem material and to Dr. Theodore S. Evans and Dr. Paul Lavietes. We wish to express our appreciation to Louis Divilio, R. T., for his completion of the films used in this study. We are also indebted to Miss Angela Brunetti for her invaluable aid in this study.

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COOLEY'S ERYTHROBLASTIC ANEMIA

SOME SKELETAL FINDINGS IN ADOLESCENTS AND YOUNG ADULTS*

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NEW YORK, NEW YORK

THE generalized skeletal lesions of severe Cooley's anemia in children have been widely observed roentgenographically since their first description during 1927.[4] Ten years later[1] we reported that skeletal changes are absent or minimal during the first year of life; and that the rarefaction characteristic of the disease during early childhood is followed by a relative sclerosis during later childhood. Prior to puberty, the most consistent and the most diagnostic changes were found in the metacarpals and femurs. In 1945, we[2] commented on the retardation of pneumatization of the paranasal sinuses.

Four patients have now been followed by us to their twenty-eighth, twenty-sixth, eighteenth and fourteenth year during periods of twenty, twenty, fifteen and eleven years respectively. The data in this report include the roentgen findings in the bones of these older patients, with comparison of early and late bone lesions in the same patient, and their changing patterns with advancing age; as well as the effects of Cooley's anemia on the cranial air sinuses, and the face and mouth.

Although Cooley's anemia and the Cooley "trait" have now been identified in large numbers of adults[10] descriptions of bone changes in older patients are few and incomplete. I have found no longitudinal studies of single individuals from early childhood through pubsecence into adult life. Apparently the changing nature of the bone lesions with advancing age has not been appreciated and the inhibitory effects of Cooley's anemia on penumatization of the maxillary, sphenoidal and temporal bones have been overlooked.

As early as 1930, Mandeville[8] noted that the metacarpals were normal roentgenographically in a youth fifteen years of age who showed pronounced changes in the skull, spine, pelvis and some of the larger tubular bones. In 2 of his patients, aged fifteen and eleven years, it is evident, in illustrations of the cranium, that the maxillary and sphenoidal sinuses had failed to pneumatize.

C. H. Smith[9] found no changes in the "metacarpals, metatarsals and other small bones" of a patient eighteen years of age whose skull exhibited diagnostic changes. Pneumatization of the cranial air sinuses of this patient appears to be normal. In a twenty year old Italian with moderate Cooley's anemia without erythroblastosis, Dameshek[5] depicts a large costal osteoma; in the calvarium changes characteristic of the disease are present, while the metacarpals appear normal or only slightly affected. "Morbo di Cooley,"[7] an Italian monograph published in 1948, contains no information on the skeletal changes during and after puberty.

CASE REPORTS

CASE 1. T. L., a girl of Greek parentage, had a normal birth and was considered normal during the first weeks of life. A brother, one year older than herself, was normal. "A few weeks" after birth she became weak, anemic and failed to thrive. Blood transfusions were given during the sixth and twelfth months at another clinic. At two and a half years, when a third blood transfusion was given, the mother was told that her daughter suffered from Cooley's anemia. The child appeared at the Babies Hospital for the first time when she was three years of age and complained of a discharging ear of six weeks' duration. Physical examination disclosed a purulent discharge in the left ear, pallor, jaundice, rodent-like face, and malocclusion of the jaws due to overbite of the swollen upper

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maxilla, cardiac enlargement and a systolic cardiac murmur, spleen enlarged into the pelvis and moderate enlargement of the liver. Dental examination showed that the teeth in the enlarged upper maxilla were normal but widely spaced. Similar oral and dental changes have been described in the patient of Cohen and Baty.[3] Hemoglobin content was 6.2 grams per 100 cc.; red blood cells numbered 3 million per cu. mm. and there were 2,200 nucleated erythrocytes per cu. mm.

Treatment with blood transfusions was begun immediately and they were given with increasing frequency later, as more blood became available. During her fourth year she received 1,700 cc. of blood in 10 transfusions; during her fifth year, 1,700 cc. in 9 transfusions; sixth year 3,200 cc. in 15; seventh year, 4,400 cc. in 18; eighth year, 4,800 cc. in 19; ninth year, 6,000 cc. in 17; tenth year, 12,600 cc. in 31; eleventh year, 8,300 cc. in 19; twelfth year, 12,000 cc. in 24; thirteenth year, 10,300 cc. in 21; and during her fourteenth year, 9,000 cc. in 19 blood transfusions. A total of approximately 70,000 cc. of blood was given in 183 transfusions which approximates an average of 400 cc. at intervals of about three weeks. Between transfusions the hemoglobin content fell to low levels of 4 to 6 grams per 100 cc. and then increased to 10 to 14 grams per 100 cc. after the transfusions.

Her nutrition was never good and she grew slowly. She had many respiratory infections. She remained weak and became fatigued easily, except for several days directly after blood transfusions. Pallor, jaundice and splenomegaly all persisted. The cardiac shadow, however, became smaller and remained normal and the cardiac murmur was heard inconstantly. The facial deformities, due to enlargement of the upper maxilla and malar bones, persisted and became more conspicuous with advancing age (Fig. 1, *A*, *B*, *C*). There was no permanent improvement of the blood despite the transfusions.

Roentgen Findings. During early childhood the tubular bones of the hands showed marked classical changes: swelling of their medullary canals and external contours, cortical atrophy and coarse porous rarefaction. During late childhood these bone changes began to diminish and had disappeared completely by the thirteenth year (Fig. 1, *D*, *E*).

The femurs at three years showed the same swelling, cortical atrophy and irregular rarefaction but at thirteen years the femurs were normal in size, shape, texture and density (Fig. 1, *F*, *G*).

The skull during childhood exhibited the characteristic dilatation of the diploic space, atrophy of the outer table and granular rarefaction without radial striation; but, at twelve and fourteen years, the changes in the calvarium had increased (Fig. 1, *H*, *I*) in contrast to the late subsidence of the changes in the hands, legs and thorax. Pneumatization of the frontal, ethmoidal and temporal bones was normal; however, the air spaces of the maxillary and sphenoidal sinuses failed to develop (Fig. 1, *J*, *K*). Normal temporal pneumatization is shown in Figure 1*E*.

In the thorax at three years, all bones showed severe swelling and porous rarefaction; the same bones at thirteen years were normal roentgenographically (Fig. 1, *M*, *N*). The first and second ribs on each side were incompletely segmented and deformed at their sternal ends; on the right side there always was a large osteoma (arrow) in the apex of the right hemithorax, apparently attached to the deformed ribs. This lesion is not unlike the costal osteoma of Dameshek's patient;[5] costal osteomas are rare in Cooley's anemia and have been described apparently in but these 2 patients.

The spine and pelvis at fourteen years, in contrast to the bones of the hands, legs and pelvis, showed severe streaky rarefaction (Fig. 1, *O*, *P*).

Summary. In this patient, the changes in the ribs and bones of the extremities regressed after the tenth year; there was no regression of similar changes in the skull, spine and pelvis. Pneumatization progressed normally in the frontal, ethmoidal and temporal bones; in contrast, pneumatization failed in the upper maxilla and body of the sphenoid.

Case II. R. R., son of Italian parents, was born after a normal delivery. At birth, he weighed 2,200 grams. Enlargement of the spleen was first detected at the eighth month; four months later it extended to the left iliac crest. Pallor, jaundice and mongoloid facies also became evident at this time. The hemoglobin content at one year was 7.3 grams per 100 cc. and the red blood cells numbered 3.3 million per cu. mm. with 8,600 nucleated red blood cells per cu. mm. During early childhood splenomegaly, pallor, slight jaundice, mal-

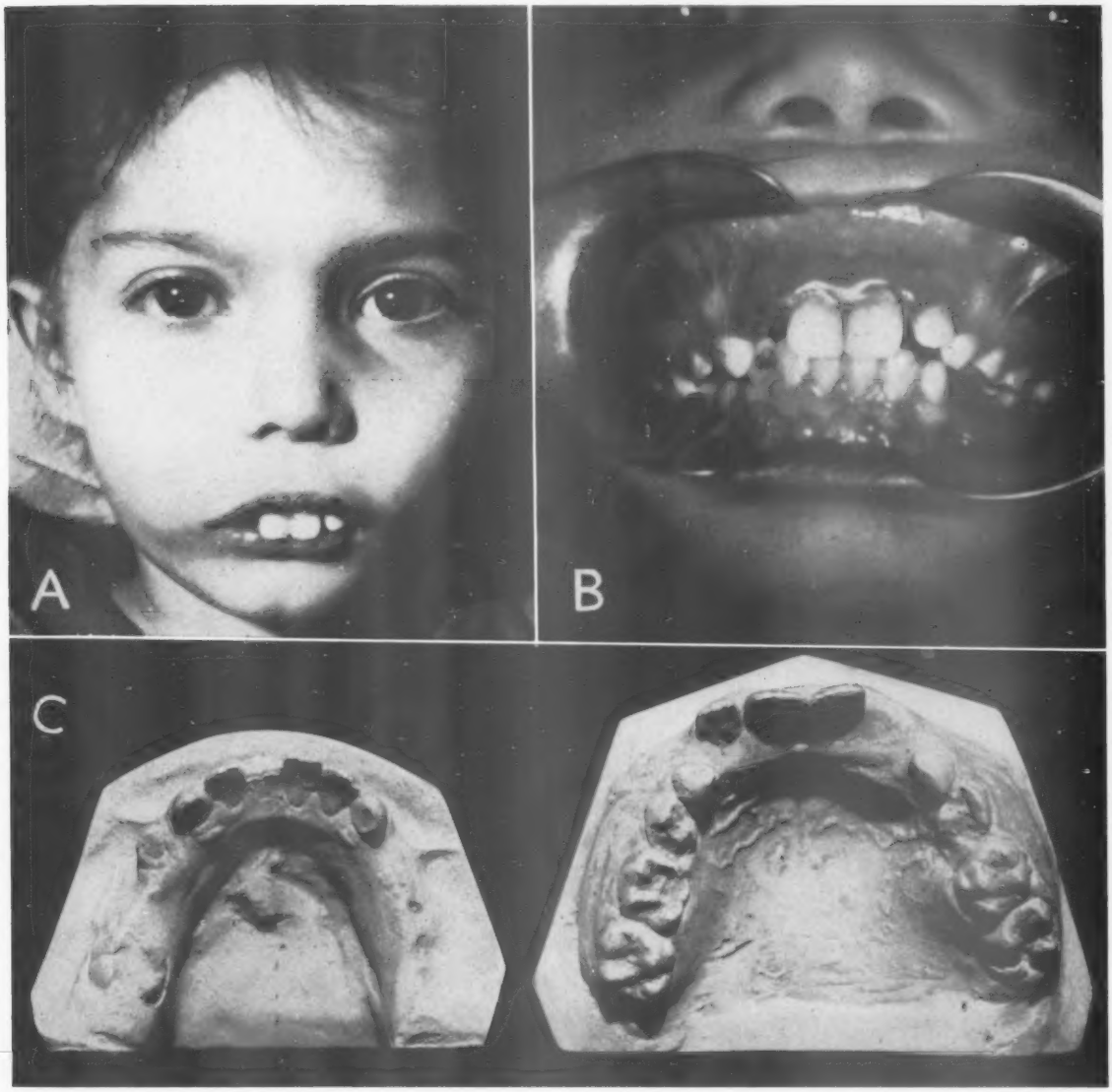

Fig. 1, (*A*) (*B*) (*C*) Case 1. (*A*) Facies at fourteen years. Ventral protrusion of the upper central incisors, with retraction of the upper lips over the enlarged upper maxilla, produces a squirrel-like appearance. Owing to the swelling of the upper maxilla, the distance between the upper lip border and the nose is increased and the nose is flattened and stretched lateral on both sides. Lateral displacement of the orbits in the enlarged upper maxilla has increased the interorbital distance and produced ocular hypertelorism. (*B*) Photograph of the mouth with lips retracted by speculum at eight years. Malocclusion of the jaws, due to overbite of the enormously enlarged alveolar ridge of the upper maxilla on the smaller alveolar ridge of the mandible, is evident. (*C*) Plaster casts of the jaws at eight years show absolute and relative hypertrophy of the upper maxilla in comparison with the smaller mandible; and spreading of the teeth in the enlarged upper maxilla.

nutrition and weakness persisted, although transfusions caused temporary remissions in pallor and weakness.

Blood transfusions were started during the sixteenth month and were given in the following schedule: second year, 2,500 cc. in 12 transfusions; third year, 3,800 cc. in 16; fourth year, 1,500 cc. in 6; fifth year, 1,500 cc. in 6; sixth year, 2,000 cc. in 8; seventh year, 2,100 cc. in 7; eighth year, 2,400 cc. in 9; ninth year, 3,600 cc. in 15; tenth year 4,500 cc. in 15; eleventh year, 3,700 cc. in 10; twelfth year, 5,800 cc. in 14;

thirteenth year, 6,900 cc. in 16; fourteenth year, 10,000 cc. in 20; fifteenth year, 12,000 cc. in 24; and sixteenth year, 6,600 cc. of blood in 14 transfusions. From the second year through the sixteenth year he received 69,000 cc. of blood in 192 transfusions; an average transfusion of 360 cc. every three to four weeks. During this time the hemoglobin content varied between 4 and 10 grams per 100 cc. and the red blood cells between 2 and 4 million per cu. mm.

During the thirty-seventh month his spleen was removed; it weighed 675 grams and showed microscopically much congestion of the pulp with much extramedullary blood formation. Both the spleen and neighboring lymph nodes showed hemosiderosis.

The tuberculin skin test was negative in the thirty-seventh month but positive in the forty-sixth. Calcifying cervical lymph nodes were visible in films made during the sixty-fifth month and these calcifications persisted without significant change to the eighteenth year. Notwithstanding severe chronic hemolytic anemia, the primary tuberculous infection appeared to be a mild one.

He grew slowly; at eleven years he weighed 45 kilograms and was 157 cm. in height. During the sixteenth year his blood contained 7.8 grams of hemoglobin per 100 cc. He attended school regularly and did well in his studies, although between transfusions he became pale and tired easily. Transfusions increased his strength, activity, color and feeling of well being temporarily. The external genitalia and pubic hair grew normally.

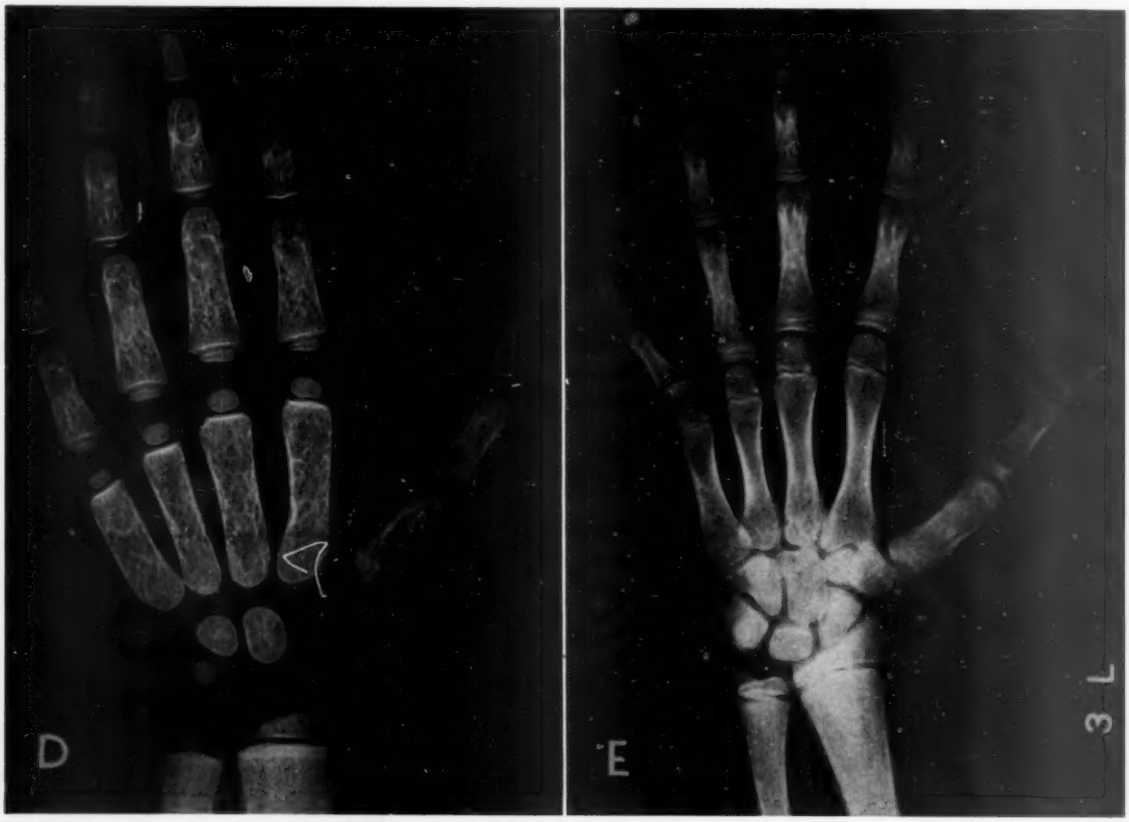

Fig. 1, (*D*) (*E*) Case I. (*D*) Hands at three years. Tubular bones all show advanced changes of Cooley's anemia; cortical atrophy, swellings of the medullary canals with obliteration of the normal external concavities of the metacarpals, and mottled generalized rarefaction. (*E*) Hands at thirteen years. The earlier erythroblastic changes have disappeared; the tubular bones are all normal roentgenographically.

The roentgen findings at all ages in the skeleton (Fig. 2, *A–H*) were similar to those in Case I with the important exceptions that in Case II the calvarium showed only slight changes at all ages, regression in the tubular

bones occurred at a slightly later age and was less complete and all parts of the temporal bones failed to pneumatize.

Case III. L. B. was a boy born of Italian parents who had apparently always been well. One sister who died of pneumonia during early childhood was said to have been jaundiced. An older brother was healthy. One older sister suffered from mild Cooley's anemia and is listed as Case IV in this report. This patient, L. B., was regarded as healthy until about the eighteenth month when pallor, jaundice and weakness developed and then persisted until he was first seen by us when he was four and a half years of age. The abnormal findings at that time included pallor, jaundice, mongoloid facies (Fig. 3, *A*, *B*), enlargement of the spleen, enlargement of the liver, cardiac enlargement and a systolic cardiac murmur. Hemoglobin content was 23 per cent and red blood cells numbered 2.1 million per cu. mm. There were 1,800 normoblasts per cu. mm.

The spleen was removed during the fifth year, following which the normoblasts increased sharply in number and remained high during the next twenty-one years, fluctuating between 8,000 and 70,000 per cu. mm. In the twenty-sixth year, normoblasts numbered 35,000 per cu. mm. Red blood cells were always diminished, varying from 2 to 3 million per cu. mm., and hemoglobin content fluctuated between 4 and 10 grams per 100 cc. Also throughout the observation period pallor, jaundice and weakness persisted although relieved temporarily by blood transfusions. Cardiac murmur persisted;

Fig. 1, (*F*) (*G*) Case I. (*F*) Femur at three years. Advanced erythroblastic changes, cortical atrophy, swellings of the external contours and the medullary canals and porous rarefaction are all evident. (*G*) Femur at thirteen years. The bone is normal; the earlier advanced erythroblastic changes have disappeared.

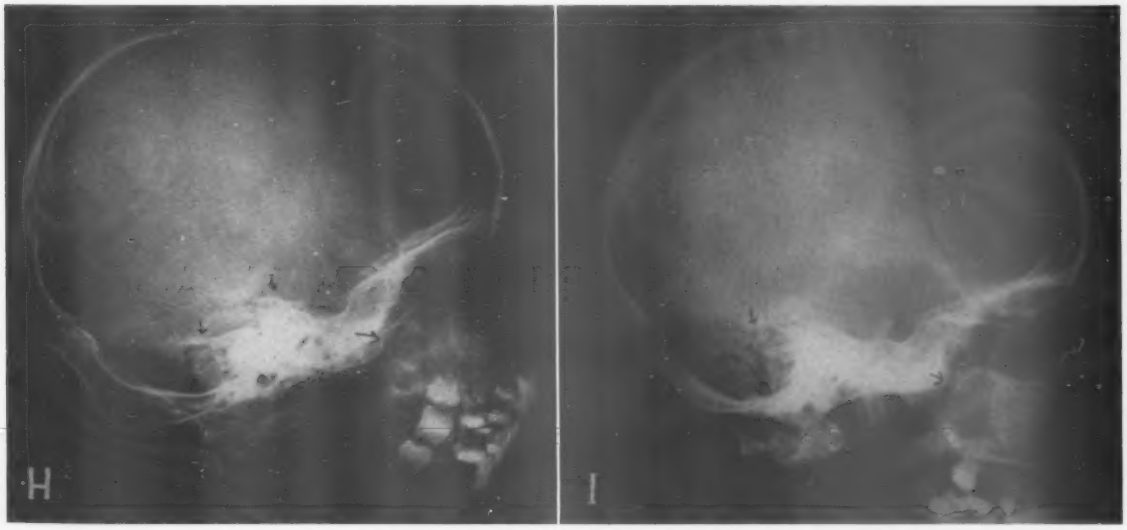

Fig. 1, (*H*) (*I*) Case I. (*H*) The calvarium at five years shows moderate deepening of the diploic space, atrophy of the external table and granular osteoporosis. (*I*) At thirteen years, all of these changes have persisted and increased. At both five and thirteen years, there are no air spaces for the maxillary sinuses.

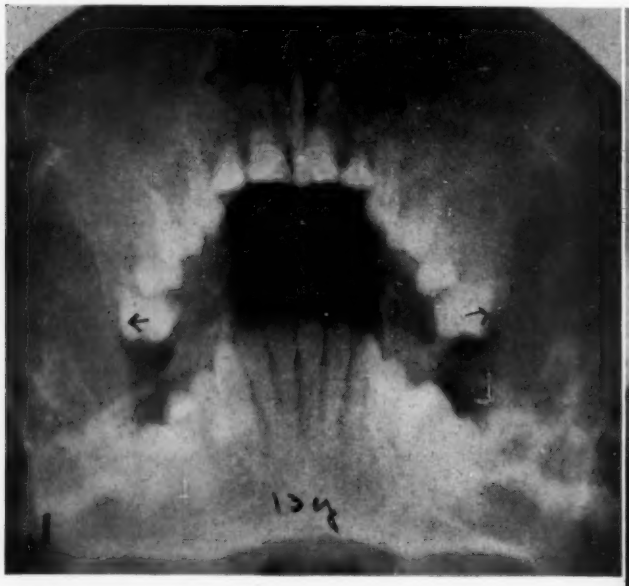

Fig. 1, (*J*) (*K*) Case 1. Frontal and lateral projection of the face at thirteen years. Pneumatization of the upper maxilla and the sphenoid bone has failed completely. The frontal sinuses are small but the ethmoidals show normal air cells. The disproportion between the enlarged upper maxilla and the mandible is evident in both frontal and lateral projections with ventral and lateral overbite of the upper teeth.

the cardiac shadow was normal or only slightly enlarged in different examinations. In the last examination in the twenty-sixth year, the cardiac shadow was normal. Impaired function of the gallbladder was demonstrated in the twenty-fifth year by cholangiography.

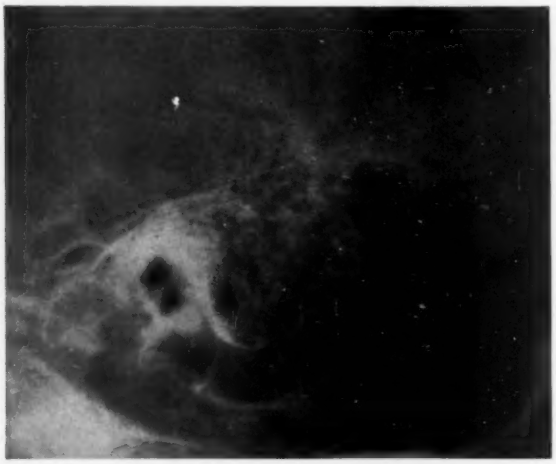

Fig. 1, (*L*) Case 1. Lateral oblique projection of the left temporal bone. Pneumatization is normal and extensive in all parts of the temporal bone in contrast to the reduced pneumatization in some of the paranasal bones. Similar normal pneumatization was present in the right temporal bone.

During the twenty-one years he received 60 transfusions which contained 32,000 cc. of blood. However, 30,000 cc. of this total was given after the eighteenth year; during the period of growth and maturation he received a negligible quantity of blood.

Despite the long standing, inadequately treated, severe hemolytic disease with slow growth and malnutrition, this boy remained cheerful and ambitious. Weakness prevented full schooling but later he held a responsible job as a checker in a shipping room and carried out this work accurately for several years. He retained a surprisingly happy disposition and a benign outlook on life. He was bright and alert mentally; when necessary, he solicited blood for himself successfully in a variety of ways. During his twenty-second year he was married; apparently his sexual activity has been normal. This is of some interest in view of the sexual infantilism reported in some of the older patients with Cooley's anemia.[6]

Roentgen findings (Fig. 3, *A–I*) were similar to those in Cases 1 and 11 with the exception

Fig. 1, (*M*) (*N*) Case 1. (*M*) The thorax at three years. The ribs, scapulas and clavicles show swollen contours with large medullary spaces, cortical atrophy and granular osteoporosis. The cardiac shadow is enlarged. (*N*) At twelve years, the bones of the thorax except the first two ribs on both sides and the cardiac shadow are normal roentgenographically. At both ages there is incomplete segmentation and deformities in the sternal ends of the first and second ribs on both sides. On the right side, there is a large mass of bone density (arrow) which seems to extend off the deformed first and second ribs and bulge into the right lung. Dameshek[5] described a similar osteoma attached to the sixth right rib of one of his patients.

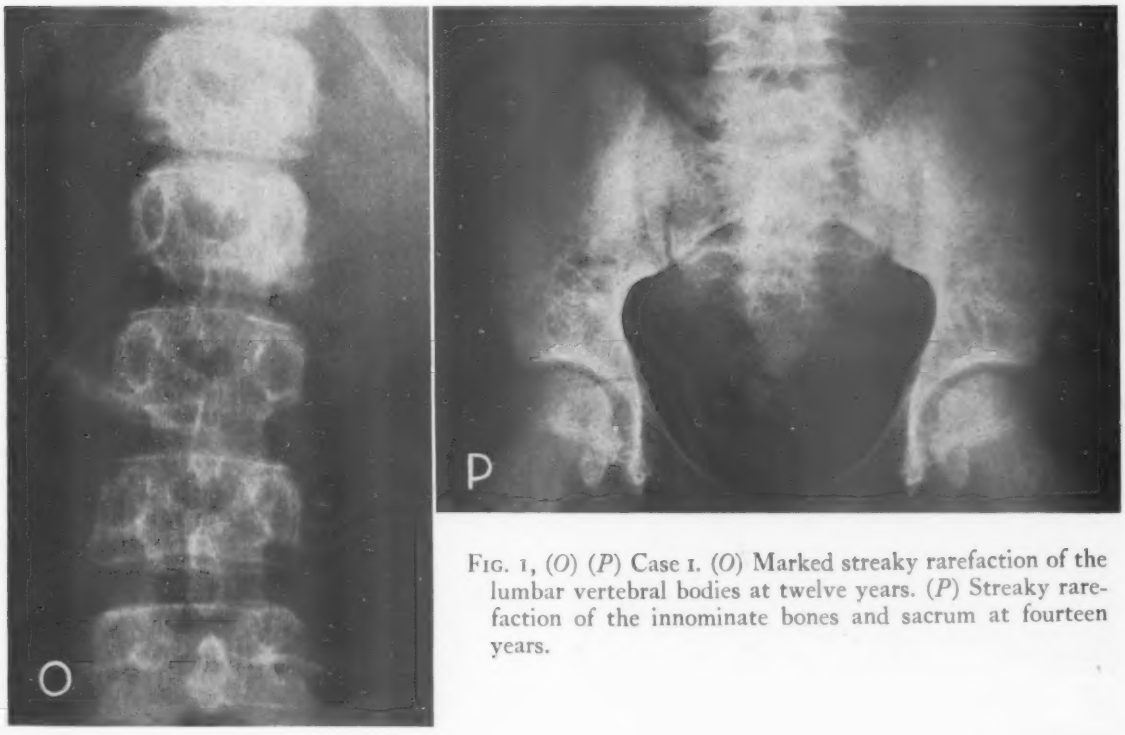

Fig. 1, (*O*) (*P*) Case 1. (*O*) Marked streaky rarefaction of the lumbar vertebral bodies at twelve years. (*P*) Streaky rarefaction of the innominate bones and sacrum at fourteen years.

that regression in the long bones occurred at a much later age and was less complete. Pneumatization of the temporal bones was severely retarded; in the upper maxilla, however, retardation of pneumatization was not as marked as in Cases 1 and 11.

Case iv. M. B., older sister of L. B. (Case iii), was first examined when eight years of age. At the time she had no complaints and came to the hospital only because hemolytic anemia had been detected in her brother. More detailed questioning later disclosed that for several years she had had occasional attacks of mild abdominal pain. The only abnormality found in physical examination was an enlarged spleen which extended 5 cm. below the costal margin. The hemoglobin content was 60 per cent and the red blood cells numbered 3.8 million per cu. mm. with 190 normoblasts per cu. mm. There was considerable anisocytosis and polychromatophilia. From the eighth to the fifteenth years, the red blood cells increased, without benefit of blood transfusions, to 5.8 million per cu. mm., and the hemoglobin to 80 per cent. During these five years, the greatest number of normoblasts recorded in 38 different counts was 350 per cu. mm.; in 17 examinations there were no normoblasts in the peripheral blood. The spleen remained large during this period and she suffered occasional mild attacks of pain in the splenic region.

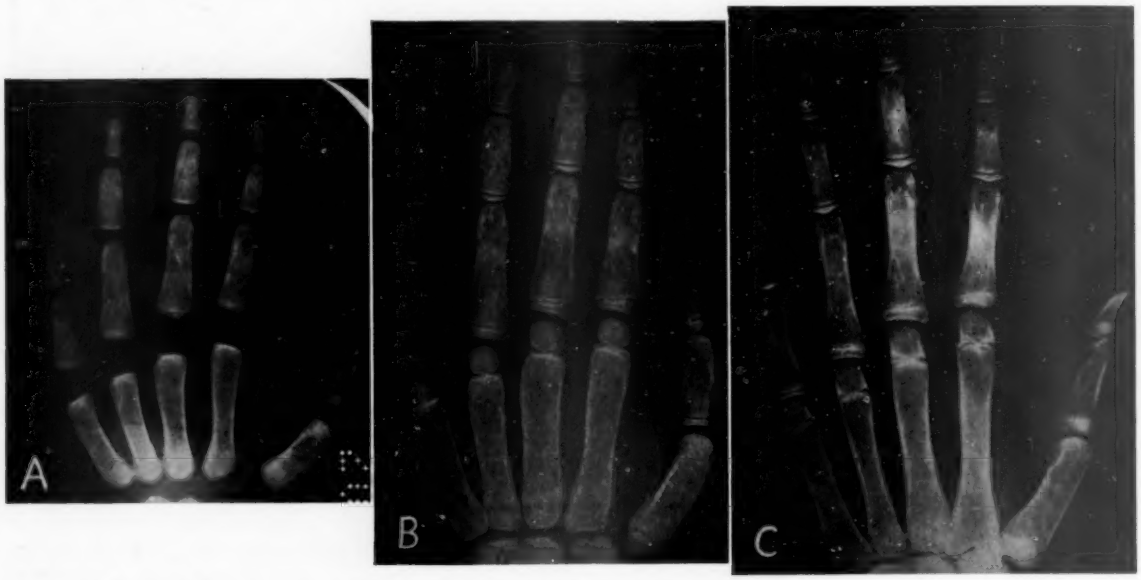

Fig. 2, (*A*) (*B*) (*C*) Case ii. (*A*) Bones of the hands at three years; the shafts show moderate swelling and cortical atrophy without porous rarefaction. (*B*) At nine years, all changes have become more marked with the addition of severe patchy cortical atrophy and spongy rarefaction. (*C*) At sixteen years, a marked regression of all of the earlier changes is evident.

Fig. 2, (*D*) Case ii. Maxillary sinuses at sixteen years are very small, approximately 1 cm. in transverse and longitudinal diameters. There was a similar retardation of sphenoidal pneumatization but the ethmoidal air cells were normally developed on both sides. Frontal sinuses were small.

From the thirteenth to the twenty-second year, when her red blood cells varied between 3.5 and 4.5 million per cu. mm., she led a normal life as a school girl and later as a factory worker. She married in her twentieth year. In the twenty-second year, an incomplete abortion required curettage of the uterus. During her twenty-fifth year she became pregnant a second time and gave birth to an apparently normal full-term daughter at another hospital. She is said to have been healthy until the third trimester of this pregnancy when her red blood

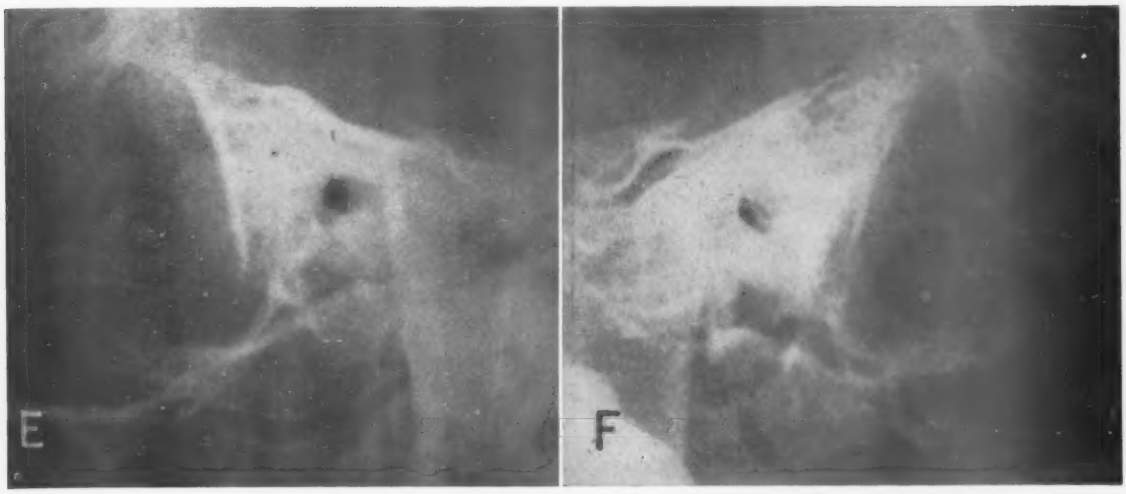

Fig. 2, (*E*) (*F*) Case 11. The temporal bones at sixteen years; right (*E*) and left (*F*). Pneumatization failed completely in the mastoid, zygomatic and squamosal segments of the temporal bones. There were, however, many cells in the bases of the petrous pyramids.

cell count fell suddenly. She had never been transfused until a few days before delivery when five blood transfusions were given.

After parturition, the red blood cell count remained low; she was transfused twice with blood during the fifth postpartum week. Nausea, fever and severe paroxysmal abdominal pain began two days after these transfusions. At this time, when we first saw her again, she exhibited pallor, jaundice and a large tender spleen. The liver edge was felt 2 cm. below the costal margin but the liver was not tender. Red blood cells had fallen to 1.4 million per cu. mm. and hemoglobin content to 4 grams per 100 cc. During the next nineteen days she was transfused several times, the red blood cells increased to 3.2 million per cu. mm. and the hemoglobin content to 8.4 grams per 100 cc. Opaque biliary calculi were visible in films of the abdomen. She improved clinically but a "drawing sensation" persisted in the splenic region. The cause of the earlier fever, anemia and splenic pain was not satisfactorily identified but splenic infarction seemed the probable causal mechanism.

When she returned two and a half months later, hemoglobin content had fallen from 8.8 grams to 4.7 grams per 100 cc. and Coombs' test was positive. Blood transfusions gave no relief from weakness, dyspnea and pain in the left upper abdominal quadrant. The spleen was removed after seven blood transfusions. Multiple adhesions bound the spleen to the diaphragm and other neighboring structures. The spleen was studded with scars of old infarcts and there was a large fresh infarct in the medial

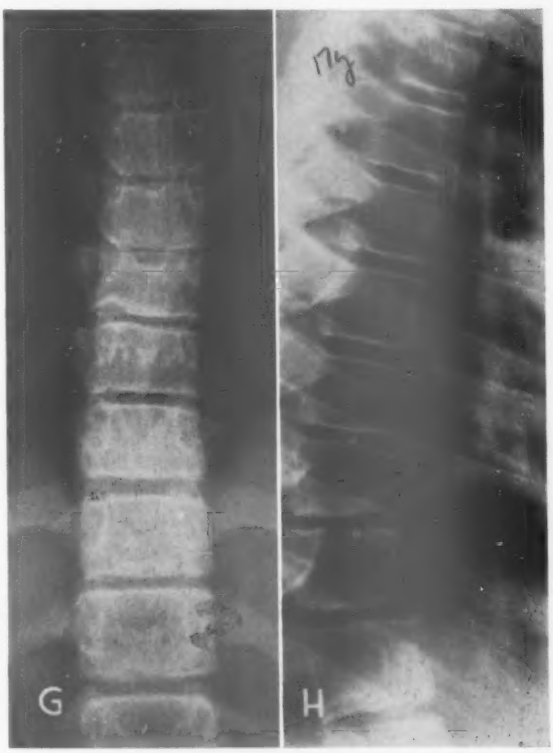

Fig. 2, (*G*) (*H*) Case 11. Thoracic spine at seventeen years; (*G*) frontal and (*H*) lateral projections. At all levels the vertebral bodies show severe reticulated rarefaction with most of the streaks running in the direction of the longitudinal axes of the spine.

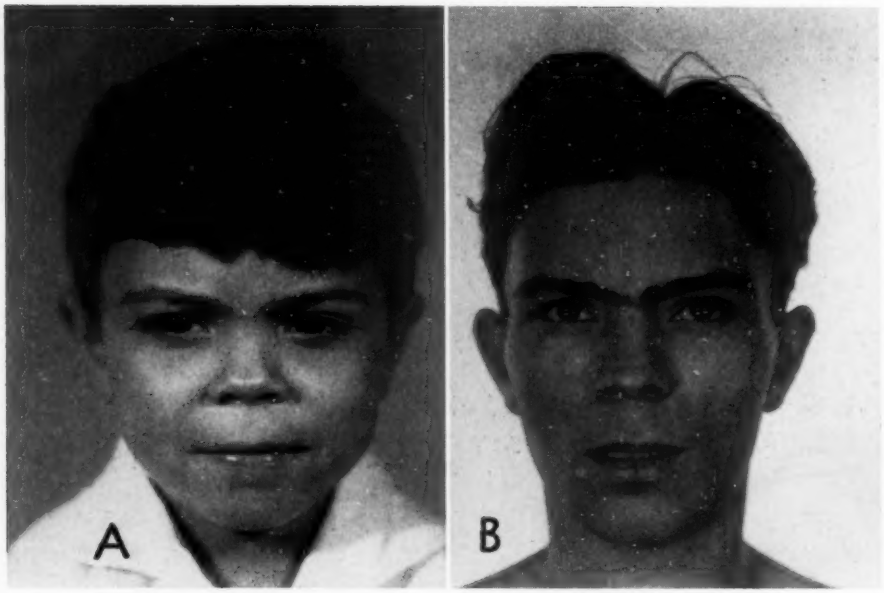

Fig. 3, (*A*) (*B*) Case III. Facies at five years (*A*) and twenty-six years (*B*). During childhood there was a strong mongoloid cast to the facies which lessened as the patient became older. This patient never showed the malocclusion or "rodent face" which was present in Cases I and II. The upper lip, however, is long and there is moderate ocular hypertelorism; both deformities are probably secondary to hypertrophy of the upper maxilla.

Fig. 3, (*C*) (*D*) (*E*) Case III. Bones of the hands. (*C*) At sixteen years advanced changes, swelling of the shafts and their medullary canals, cortical atrophy and spongy rarefaction are all still present. (*D*) At twenty-two years, these changes have lessened substantially, especially cortical atrophy. (*E*) At twenty-five years, the changes are still present in slight degree but are improved in comparison with those at twenty-two years.

segment of the superior splenic pole which was adherent to the liver. Several small accessory spleens were found in the splenic pedicle. Post-splenectomy course has been uneventful for eight months up to this writing, save for occasional severe headaches. Her blood im-

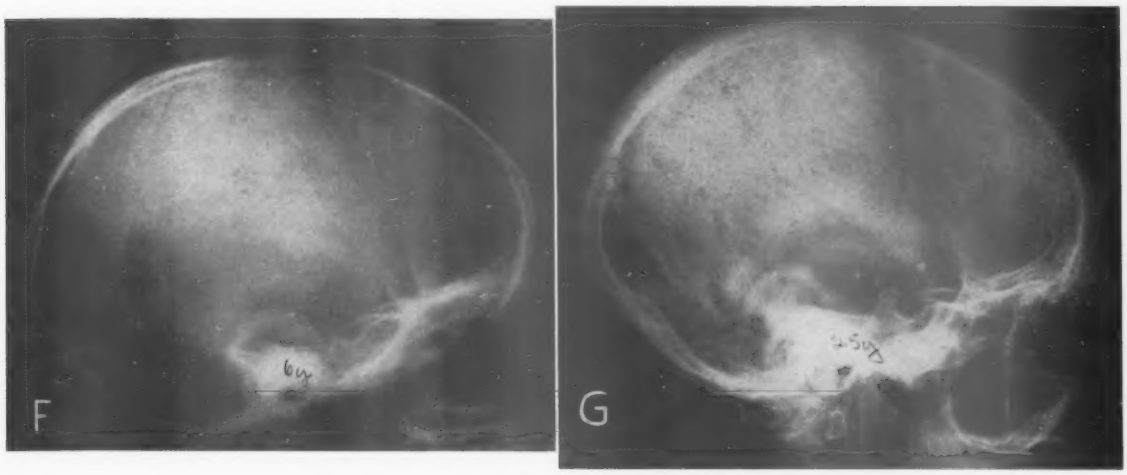

Fig. 3, (*F*) (*G*) Case III. Lateral projections of the skull. (*F*) At six years, the only change suggestive of Cooley's anemia is moderate widening of the diploic space in the inferior segment of the frontal squamosa. (*G*) At twenty-five years, the entire diploic space of the frontal and parietal bones is widened and there is a severe granular osteoporosis. Compare the late increase in the cranial changes with concurrent regression of the manual changes.

proved and in the last examination there were 4 million red blood cells per cu. mm., with 6,300 nucleated red blood cells per cu. mm. The hemoglobin content was 10 grams per 100 cc. There were many target cells and many deformed red blood cells.

The infant daughter appeared to be healthy until the fifth month when the blood became abnormal. At eight months the hemoglobin content is 8 grams per 100 cc. and the spleen extends 3 cm. below the ribs. The infant's skeleton is normal roentgenographically. The development of Cooley's anemia in this daughter of a mother who is known to have had mild Cooley's anemia since her eighth year has borne out our prediction made in 1937 (ref. 1, page 303) that adults with mild Cooley's anemia might transmit the disease to their offspring. Actually it was the study of this patient, M. B., which gave rise to this surmise, which has come true after thirteen years.

The roentgen findings are shown in Figure 4, *A–E*. The bones of the extremities were normal at all ages. The moderate changes in the skull

Fig. 3, (*H*) Case III. Small, rounded juvenile type of maxillary sinuses at twenty-five years. The superior orbital fissures on both sides and the foramen rotundum on the right are normal in size. In our studies of the foramens and clefts in the base of the skull, there was no evidence of reduction in their sizes secondary to swelling of contiguous bone. It seems probable that there is little or no marrow activity in the bones on the margins of the basilar cranial foramens and clefts.

Fig. 3, (*I*) Case III. Streaked rarefaction of swollen pelvic bones, and lumbar and sacral segments of the spine at twenty-two years.

during childhood became more marked with increasing age. All of the paranasal sinuses were small save the ethmoidals. In the temporal bones there were no air cells in the mastoid, zygomatic and squamosal portions but there were air cells in the bases of the petrous pyramids. The slight changes in the ribs during childhood increased to moderately severe changes during the third decade. The cardiac shadow was never enlarged. At twenty-seven years the pelvic bones and vertebrae showed moderately severe reticulated rarefaction.

Case v. A. M., male, Greek, aged fifty-three, was admitted to the Presbyterian Hospital with the complaint of weakness of several months'

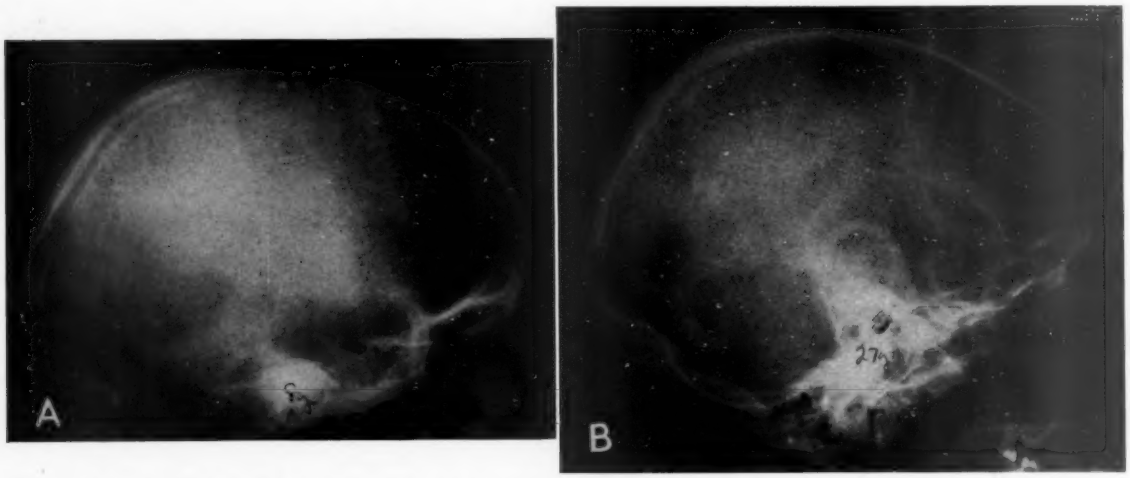

Fig. 4, (*A*) (*B*) Case iv. The calvarium at eight years (*A*); there is slight widening of the diploic spaces in the frontal and parietal bones. At twenty-seven years (*B*), diploic widening is now greatly increased in frontal and parietal bones, the outer table is atrophic, and there is a severe generalized porous rarefaction.

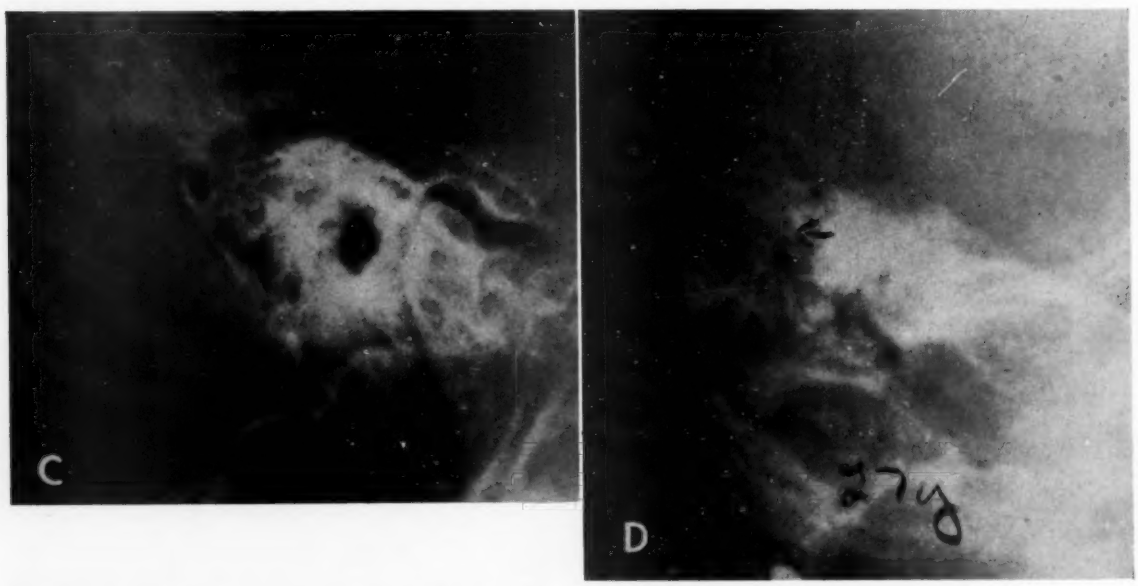

Fig. 4, (*C*) (*D*) Case iv. Right temporal bone at twenty-seven years. (*C*) Lateral oblique projection shows absence of air cells in the squamosa, mastoid process and zygomatic process. Many air cells are, however, visible in the base of the petrous pyramid. (*D*) Frontal projection of the petrous pyramid shows small cell pneumatization of its base. There was a similar pattern of retarded pneumatization in the left temporal bone.

duration. Examination disclosed splenomegaly and "target cells" phenomenon with anisocytosis. Roentgenographically there were no abnormal changes in the skeleton except deficient pneumatization of the right maxillary sinus and the left temporal bone.

Fig. 4, (*E*) Case iv. Streaky rarefaction of iliums, sacrum, and inferior lumbar spinal vertebras at twenty-seven years.

COMMENT

In the distal portions of the skeleton—hands, arms and legs—in Cases i, ii and iii, the bone lesions regressed during late childhood. In these same patients during the same time, similar bone changes persisted and even increased in the central portions of the skeleton—the calvarium, spine and pelvic bones. The skeletal changes in Cooley's anemia are due, primarily, to overactivity and overgrowth of the bone marrow. Their distal regression, and central persistence with advancing age, follows the pattern of regression of normal marrow as age increases, from the distal portions of the skeleton toward the trunk. According to Wintrobe,[11] in a normal person eighteen years of age, active marrow is found only in the vertebrae, ribs, sternum, skull, pelvic bones and, to a lesser degree, in the proximal epiphyses of the femurs and humeri; in the more distal portions of the skeleton active red marrow has been replaced with inactive fatty marrow.

In Cases i and ii, regression became evident first during the pubescent period. In Case iii, regression was considerably slower and less complete. It is possible that the earlier and more frequent giving of blood transfusions to the first and second patients stimulated earlier regression of their bone lesions. The earliest and most complete regression occurred in Case i, a female, which suggests that earlier activity of the female pubescent hormonal factors may have been responsible. In all patients regression occurred in the ribs but it was not as early or as pronounced as in the tubular bones of the extremities.

In Case iv, an exceedingly mild example of the disease both clinically and hematologically, the distal portions of the skeleton were normal roentgenographically both early, eighth year, and late, twenty-eighth year. In the central segments of this patient's skeleton, especially the spine and the skull, the bone changes became more conspicuous as age increased, although the peripheral blood of this patient was practically normal until her second pregnancy during her twenty-fifth year.

Pneumatization of the cranial air sinuses was retarded in pronounced degree in all patients but not all of the sinuses were affected in any patient. Inhibition of pneumatization was evident when these patients were first examined by us, in one case as early as the fourth year. Retardation of pneumatization became more conspicuous and more certain as age increased. The maxillary and sphenoidal sinuses were small in all patients; in Cases i and ii the maxillary and sphenoidal sinuses were practically obliterated. The frontal sinuses were small in all patients but they were not as retarded as the maxillary and sphenoidal sinuses; pneumatization of the frontal sinuses of normal persons shows such wide variations in size and shape that accurate estimation of the degree of retardation in these patients with Cooley's anemia was difficult. The ethmoidal cells were all normally pneumatized, which suggests that there is little or no marrow activity in the ethmoidal bone.

Pneumatization of the temporal bones

failed almost completely in Cases II, III, and IV in the mastoid, zygomatic and squamous segments; in Case II there were no air cells in the petrous pyramids as well. In contrast, pneumatization of the temporal bones was normal in Case I, a severe example of the disease in all other respects. This may signify that the marrow activity in the temporal bones of different individuals varies substantially. In Case IV, a mild form of Cooley's anemia in which the tubular bones of the extremities were normal at all ages, pneumatization of the temporal bones was almost completely inhibited.

The disproportionate overgrowth of the upper maxilla with ventral and lateral extension of its alveolar ridge may produce serious malocclusion of the jaws (Cases I and II). Ventral protrusion of the upper central incisors with retraction of the upper lips and overbite on the lower jaw may give rise to rodent facies in older patients which is more common and more diagnostic of Cooley's anemia than the mongoloid facies characteristic of Cooley's disease in some younger children. Owing to marked swelling of the upper maxilla in some patients (Cases I and II) the orbits are shifted laterally and the interorbital distance increased to a degree which produces significant ocular hypertelorism; this is a clinical sign of Cooley's anemia which has not been sufficiently appreciated in the descriptions of both younger and older patients.

SUMMARY

Four patients with Cooley's anemia were studied over long periods, from early childhood into the second and third decades.

Lesions in the tubular bones of the extremities regressed with increase in age while the changes in the central segments of the skeleton persisted and increased. Regression first became evident near the beginning of pubescence.

Pneumatization of the paranasal or temporal bones was retarded in all patients.

Overgrowth of the upper maxilla leads to serious malocclusion of the jaws and a rodent facial appearance in some patients.

After puberty, the central portions of the skeleton—skull, spine and pelvic bones—are the optimal sites for demonstration of roentgenographic changes in bones. The bones of the hands, the optimal sites for the roentgen demonstration of Cooley's anemia in children, are the poorest sites after puberty.

Retarded pneumatization of cranial air sinuses appears to be a common phenomenon in both infantile, juvenile and adult patients.

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GASTROINTESTINAL ROENTGENOGRAPHIC OBSERVATIONS IN PEPTIC ULCER PATIENTS TREATED BY VAGOTOMY*†

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IN DECEMBER, 1944,[14] when Dragstedt re-introduced vagotomy for the treatment of peptic ulcers in human beings, he re-opened the question of vagus nerve anatomy and its relation to gastrointestinal physiology. The majority of the reports on this subject which appeared in surgical and gastroenterological journals between 1945 and 1947 mentioned only good results. Subsequent reports, however, tend to be less optimistic.

The purpose of this paper is to present the effects (in 47 patients) of complete bilateral transthoracic vagotomy, without gastroenterostomy, upon peptic ulcers and upon the several subdivisions of the gastrointestinal tract demonstrated by roentgen examinations. This work, begun in August, 1946, was done at the Veterans Administration Hospital, New York City, as a combined venture of the Surgical and of the X-Ray Services.

To provide uniformity and to facilitate later evaluations, the cases were carefully selected using the following criteria:

1. The presence of chronic severe ulcer pain with or without melena. Cases with active or acute hemorrhage were excluded.
2. Roentgen evidence of duodenal or jejunal (stoma) ulcer without pyloric obstruction or gastric retention.
3. Inadequate response to prolonged medical treatment. Gastric ulcers were excluded.

All patients were males; the youngest was twenty-one and the oldest fifty-eight years of age.

Immediately before vagotomy, a gastrointestinal series which could be used for comparison with subsequent examinations was done. Careful follow-up clinical and roentgenological examinations were made at two weeks, at one, three, six, twelve, eighteen, twenty-four, and thirty months after vagotomy. The average follow-up for all of these cases was two years.

After vagotomy, a Levin tube was introduced into the stomach of each patient and continuous suction was maintained for three days. Meanwhile, parenteral feeding was given. Patients were subsequently given liquid, soft and regular diets.

The clinical results of vagotomy were tabulated as follows:

Excellent: In this group were included all cases that became asymptomatic immediately after vagotomy, without roentgen evidence of active ulcer, and without melena (Fig. 1, *A* and *B*).

Good: In this group were included all cases with modified or some residual ulcer symptoms without demonstrable ulcer or roentgen examinations.

Failure: In this group were included

TABLE I

RESULTS

Duodenal Ulcer	40 cases	
Excellent	8 cases	Together equal 67.5% of all cases.
Good	19 cases	
Failure	13 cases	
Jejunal Ulcer	7 cases	
Excellent	3 cases	
Failure	4 cases	
Total number of cases—47		
Follow-up Time—Average of 2 years		

* Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are a result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

† Presented at the Fiftieth Annual Meeting, American Roentgen Ray Society, Cincinnati, Ohio, Oct. 4–9, 1949.

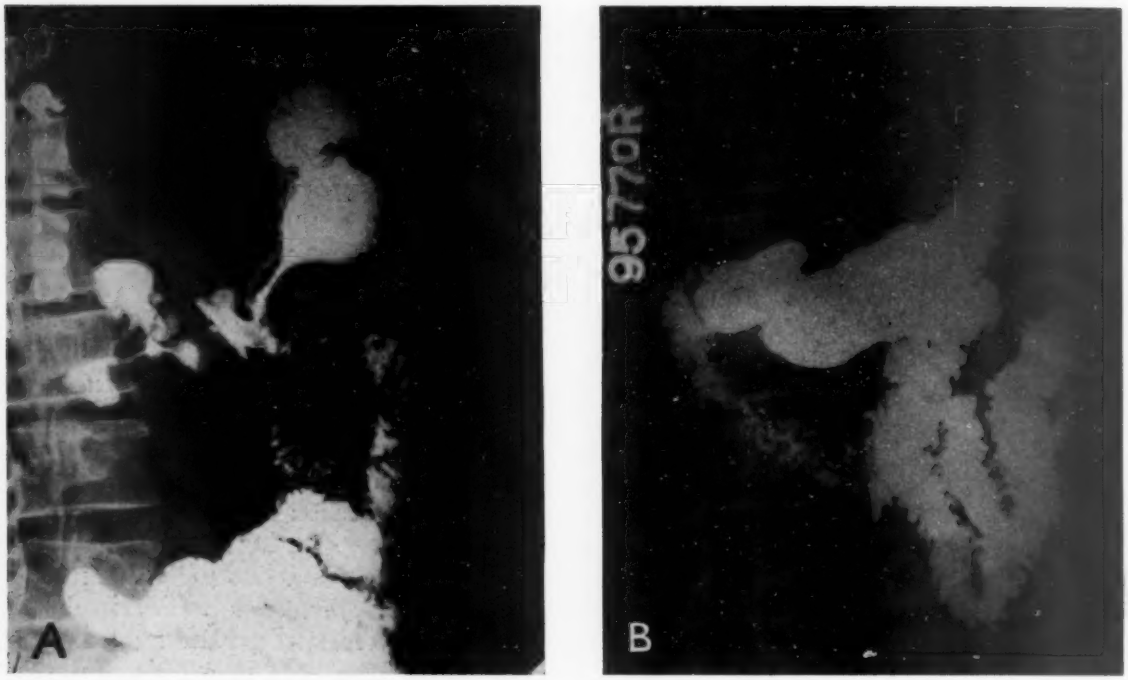

Fig. 1. Excellent results. (*A*) Pre-vagotomy—ulcer crater. (*B*) Same patient, 2 weeks post-vagotomy—normal bulb. No symptoms.

those cases with persistent and recurrent ulcers.

Vagotomy Effects on Peptic Ulcers (Table 1). In order to evaluate the effect of vagotomy on duodenal ulcers, 40 patients were studied. Preoperatively, 16 of these showed crater shadows in their roentgenograms and 24 showed deformed bulb. Irritability and spasm of the duodenal bulb, mucosal distortion and duodenitis, antritis, eccentric pyloric channel, and gastric hyperperistalsis were demonstrable

Table II

TABULATION OF PERSISTENT ULCERS

Duodenal Ulcer				Jejunal Ulcer		
Time after Vagotomy	Crater	Deformed Bulb	Non-visualized Bulb	Crater	Total	Failures
1 mo.	3	6	2	3	14	
2 mo.	0	6	2	3	11	1 (partial gastrectomy performed)
3 mo.	0	5	1	2	8	3 (partial gastrectomy performed)
6 mo.	0	2	0	2	4	1 (partial gastrectomy performed)
1 yr.	0	1	0	2	3	2 because of recurrent clinical symptoms and melena
2 yr.	0	1	0	1	1	1 (same as above)

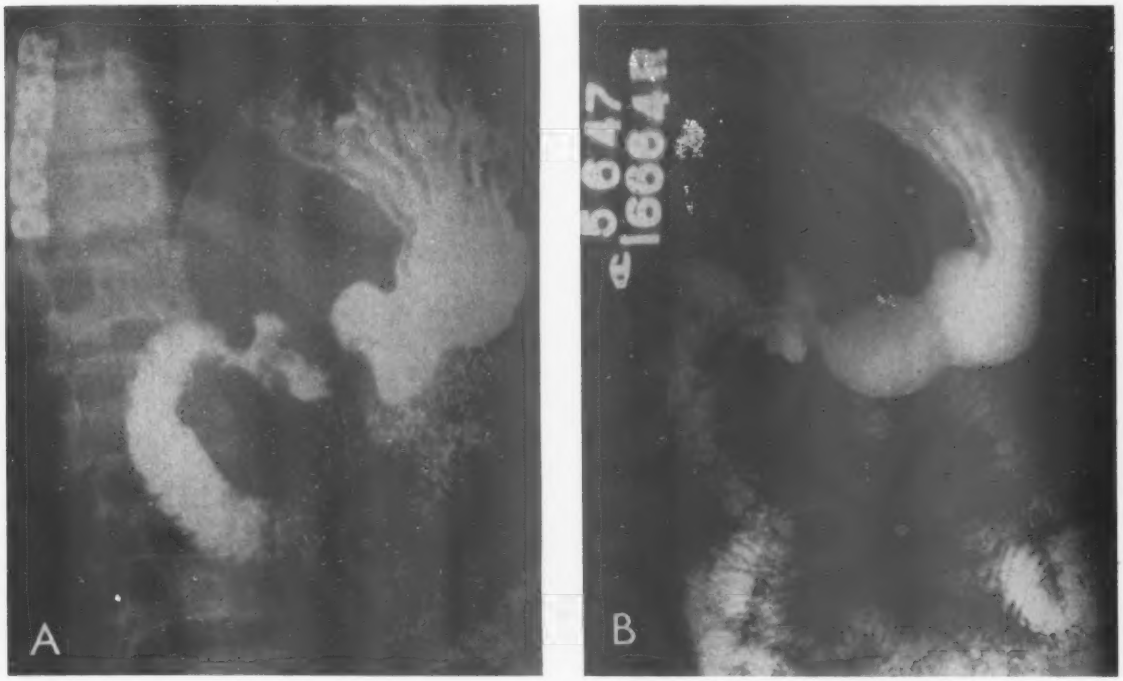

Fig. 2. Persistent duodenal ulcer at one month. (*A*) Pre-vagotomy—deformed bulb. (*B*) Same patient, one month post-vagotomy—large crater.

in many of these patients. For the sake of simplicity, the latter group will be referred to as those having deformed bulb. All of these 40 cases had ulcer symptoms, and many of them, melena.

Seven patients with jejunal ulcers were studied; each of them showed crater shadows in their roentgenograms and each had ulcer symptoms. One of these patients had a partial gastrectomy and the remaining 6 had gastroenterostomy several years before vagotomy.

Results. Immediately after vagotomy, ulcer symptoms subsided in only 36 cases. The melena disappeared in all of the cases except one. During subsequent follow-up examinations, melena re-appeared in 7 cases. Within one month, the roentgen findings in all except 11 cases showed residual deformity of the duodenal bulb or a non-deformed bulb.

Persistent Ulcers (Table II). By persistent ulcer is meant an ulcer which failed to heal during the first month after vagotomy. Under a controlled regimen, in a hospitalized patient who is removed from disturbing external influences, most peptic ulcers will heal within thirty days.

In patients with vagotomy, however, Dragstedt reported healing of peptic ulcers within three weeks.[14,15,16] Moore[40] and Smith[48] corroborated these findings. In our analysis, the more conservative time interval of one month was used, plus the presence of two criteria: (1) the persistence or slight modification of preoperative ulcer symptoms, (2) the persistence of preoperative roentgen findings.

Recurrent Ulcers (Table III). A recurrent ulcer is an ulcer which reappeared in a patient who, by clinical and roentgenographic standards, had previously shown a healed ulcer for two consecutive months after vagotomy. All patients with recurrent ulcers in this series showed ulcer craters on roentgenograms and presented active ulcer symptoms.

Non-visualized Bulb. This finding occurred in 11 duodenal cases, up to one month after vagotomy. Non-visualization of the duodenal bulb is believed due to unsatisfactory emptying of the stomach.

Whether it implies persistent ulcer in all cases cannot be stated with certainty. In 4 of these 11 cases, partial gastrectomy, two to four months after vagotomy, confirmed a persistent ulcer. All 4 had ulcer symptoms and severe gastric atony (Fig. 3). In the other 7 cases the persistence of ulcers remains unconfirmed. These 7 patients had mild to moderate gastric atony

TABLE III

RECURRENT ULCERS

10 in 47 Patients with Previous Peptic Ulcers

Duodenal Ulcer—9 (Crater—Roentgenogram)	Jejunal Ulcer—1 (Crater—Roentgenogram)
10 mo. —1	at 14 mo.
1 yr. —2	
1½ yr. —2	
2 yr. —2	
2½ yr. —2	

and became asymptomatic immediately after vagotomy. In 6 of them the bulb was again visualized at three months, and in the seventh, the bulb was visualized at six months. In each of these 7 cases, the roentgenograms were interpreted as showing residual bulb deformity caused by a previous ulcer.

Analysis of Failures—17 cases—36 per cent (Table IV). Ulcers persisting for one

TABLE IV

FAILURES

17 in 47 Peptic Ulcer Cases

Persistent ulcers— 7 cases
Duodenal ulcers— 4 cases
Jejunal ulcers — 3 cases
Recurrent ulcers—10 cases
(all after 10 months post-vagotomy)
Duodenal ulcers— 9 cases
Jejunal ulcers — 1 case

year, and ulcers requiring another operation within six months after vagotomy, were considered failures. Seven of these 17 patients had persistent ulcers (Fig. 3 and 5) and 10 of them had recurrent ulcers. In 2 of these cases, a partial gastrectomy was performed two and one-half months after vagotomy for relief of symptoms (Fig. 6). In 2 other patients, jejunal ulcers persisted for one year (Fig. 4).

Ten of the 17 patients were considered failures because of recurrent ulcers. All of these patients had active ulcer symptoms and roentgenographic findings were interpreted as active ulcers.

Incomplete vagotomy—3 cases. Persistence or recurrence of a positive insulin reaction was used as presumptive evidence for incomplete vagotomy. These 3 cases of incomplete vagotomy are excluded from the statistics given in this report. It is of interest that in each of these 3 patients, the ulcers were healed one month after operation and that in 1 of them an ulcer recurred at one year.

Complications of Vagotomy:

Pleural effusion—12 cases. All were left sided and of moderate amount. All subsided within two weeks.

Hydropneumothorax—3 cases. All were left sided and subsided within ten days.

Segmental pneumonitis—1 case. This cleared within three weeks.

Segmental atelectasis—1 case. This subsided in two days.

Pericardial effusion—1 case. This subsided within one month.

All complications referred to above were associated with minimal or no symptoms.

Deaths—2 cases. One of these patients died of pulmonary embolism twenty-four hours after partial gastrectomy made necessary for relief of gastric atony which had persisted for two months after vagotomy. The second patient died of hepatic insufficiency two weeks after gastroenterostomy, also performed for relief of gastric atony which had endured for three months after vagotomy. In this individual an extensive cirrhosis was found at postmortem.

Effects of Vagotomy on Stomach. Perhaps the most striking effect of vagotomy for man and animals alike is atony of the stomach. All cases in this particular series

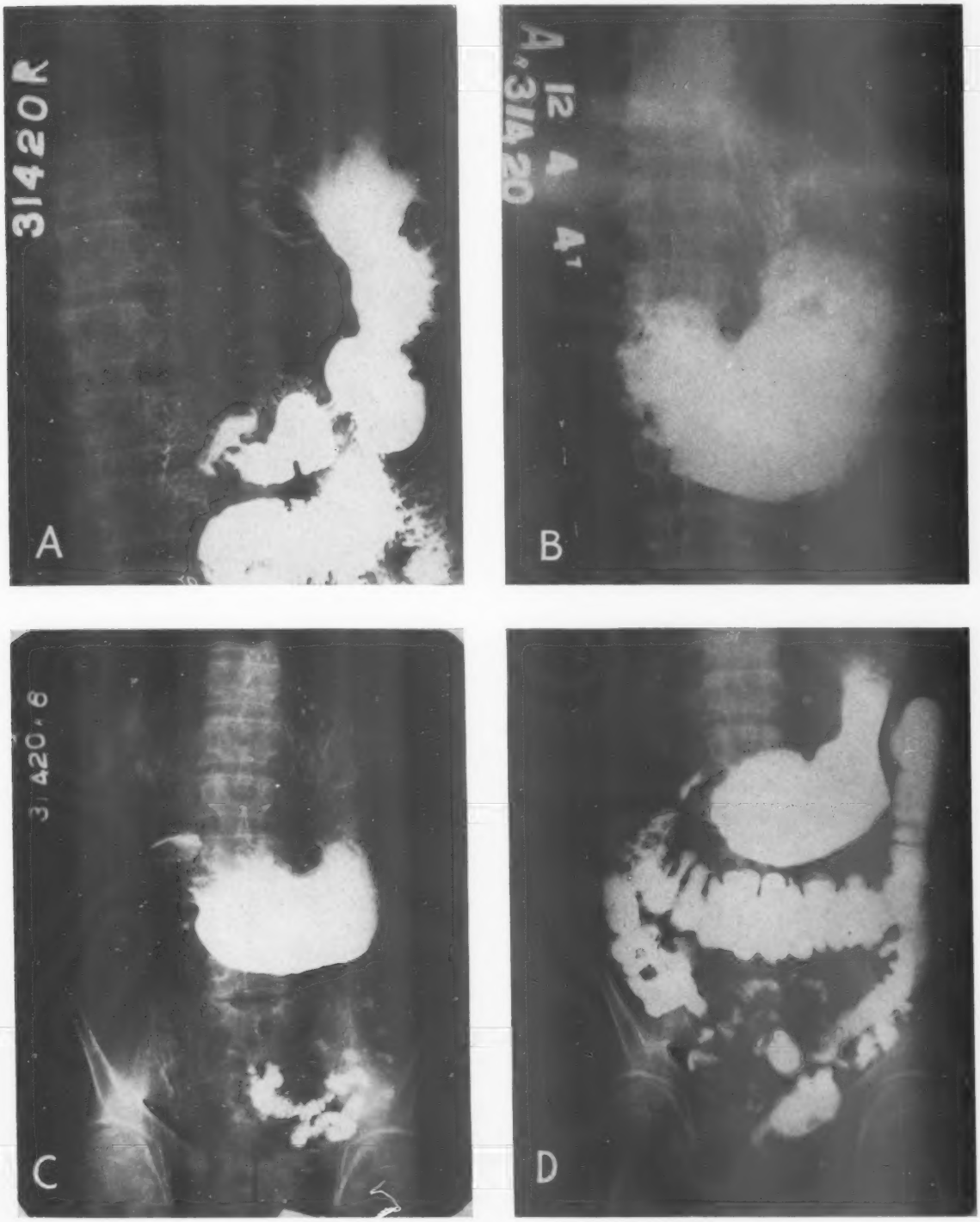

FIG. 3. Patient with persistent duodenal ulcer at three months (failure). (*A*) Pre-vagotomy, constricted bulb. (*B*) Two weeks post-vagotomy. Severe gastric hypotonicity; non-visualized bulb. (*C*) Six hour film, one and a half months post-vagotomy, large gastric residue. (*D*) Twenty-four hour film, three months post-vagotomy, large gastric residue.

of vagotomies in man fall naturally into four groups:

Group 1—No Atony. All those cases without dilatation of the stomach, without gastric residue at six hours, with normal gastric peristalsis, and without initial delayed emptying of the stomach.

Group 2—Mild Atony Group. Cases with dilatation of the stomach up to 1½ times the preoperative size, with six hour retention up to 30 per cent, and with mildly decreased frequency and depth of peristalsis.

Group 3—Moderate Atony Group (Fig. 5). Cases with dilatation of the stomach up to twice the preoperative size, with six hour retention of 30 to 60 per cent and with moderately decreased frequency and depth of peristalsis.

Group 4—Severe Atony Group (Fig. 6). Cases with dilatation of the stomach of more than twice the preoperative size, with six hour retention of more than 60 per cent, and with markedly decreased frequency and depth of peristalsis.

Table V

ATONY OF STOMACH

Duodenal Ulcers—40 Cases

Time	Mild	Moderate	Severe	Total	Per Cent
1 mo.	5	18	10	33	75
3 mo.	2	7	2	11	26
6 mo.	3	4	1	8	20
1 yr.	2	3	1	6	15
1½ yr.	2	3	0	5	12

Table v shows that following vagotomy, the majority (75 per cent) of the cases in this series developed moderate to severe gastric atony. By the third postoperative month, gastric atony was demonstrable in only 26 per cent of all patients. However, in these patients, re-establishment of normal gastric tonus required from six to eighteen months after vagotomy. A direct relationship was not demonstrable between the degree of gastric atony and the severity of such associated symptoms as foul breath, fullness and eructations. The above findings are in accordance with reports by other workers on the subject of vagotomy.[14,15,16,17,23,24,39]

Roentgenoscopically, in the majority of the cases with moderate and severe atony, the shallow and infrequent peristaltic waves were seen to expend themselves ineffectively at the pylorus, without propulsion of barium into the duodenum.

During the second and third decades of this century, many physiologists frequently found delayed emptying of the stomach to follow vagotomy in animals.[26,27,29,33] Since 1945 a great majority of surgeons have reported similar results to follow vagotomy in man.

One month after vagotomy, 13 of the patients in this series showed delayed initial emptying for as long as one hour. By the third postoperative month, only 4 of these had initial delayed emptying, and at six months normal gastric empyting was found in all cases. Except in those individuals with severe gastric atony, delayed emptying was not necessarily associated with six hour retention, or with dilatation of the stomach.

Placing a patient in the right lateral recumbent position did not facilitate initial emptying of the stomach. However, slight or moderate manual pressure on the greater curvature of the stomach readily pushed barium into the bulb, thus demonstrating that pylorospasm played no part in delayed emptying of the stomach, and that gastric atony was the chief factor in this delay. Not one case showed an elongation of the pylorus which would have suggested spasm or hypertrophy of the pyloric muscles. Re-establishment of gastric tonus, probably due to assumption of complete control by the inherent intramural nerve mechanism, varied considerably with each individual case.

Gastric Secretions. The preoperative twelve hour overnight volume of gastric secretion dropped immediately after vagotomy from an average level of 970 cc. to one of 290 cc.

Fig. 4. Persistent jejunal ulcer in same patient for one year (failure). (*A*) Pre-vagotomy, crater. (*B*) One month post-vagotomy, crater persists; stomach unchanged. (*C*) Six months post-vagotomy, crater persists; stomach unchanged. (*D*) One year post-vagotomy, crater persists; stomach unchanged.

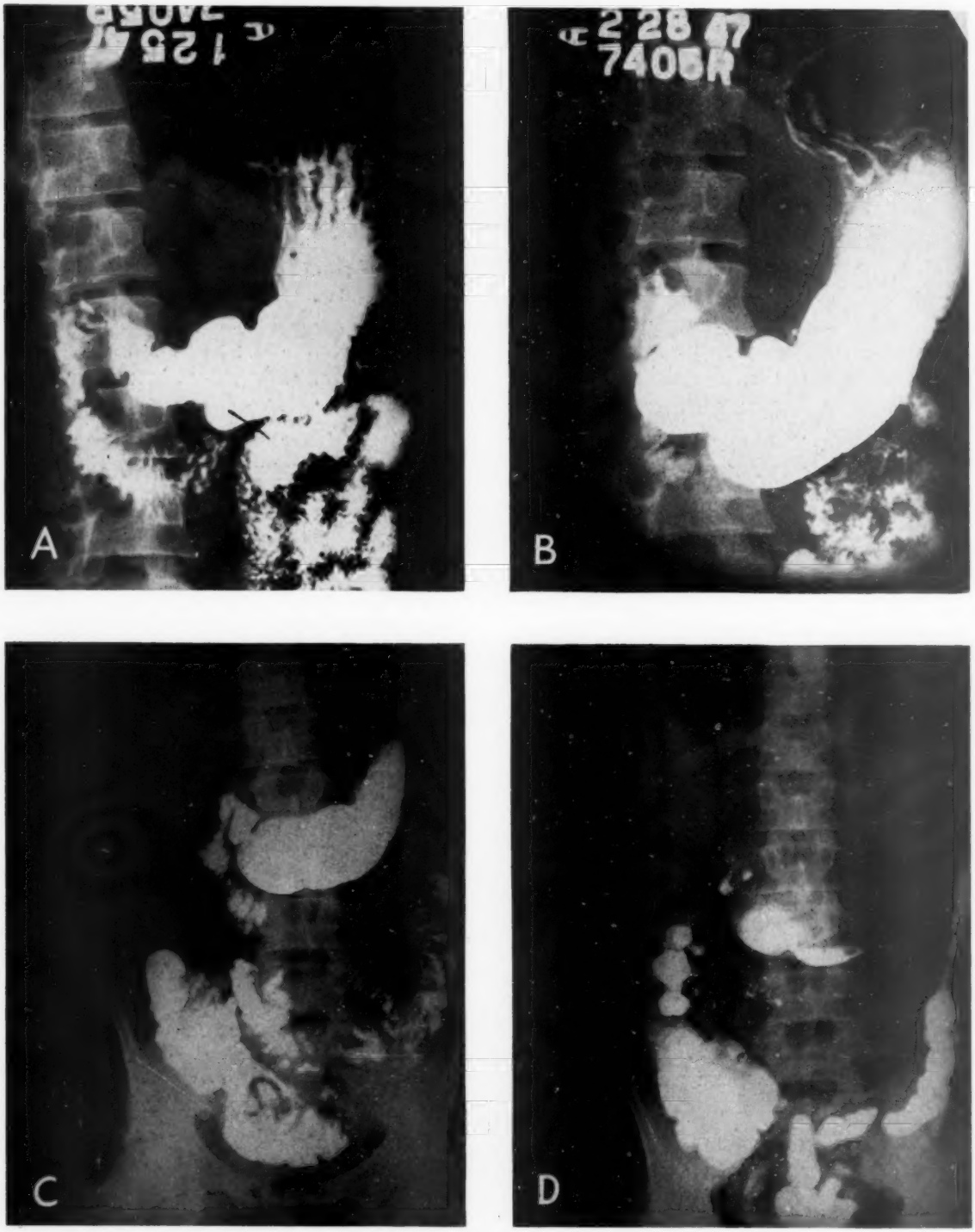

Fig. 5. Moderate gastric hypotonicity in same patient; duration three months with persistent ulcer. (*A*) Pre-vagotomy, constricted bulb. (*B*) One month post-vagotomy, bulb unchanged; stomach twice preoperative size, peristalsis shallow. (*C*) Three months post-vagotomy, five hour film. Residue in stomach between 30–60 per cent. (*D*) Three months post-vagotomy, twenty-four hour film. Residue in stomach 10 per cent.

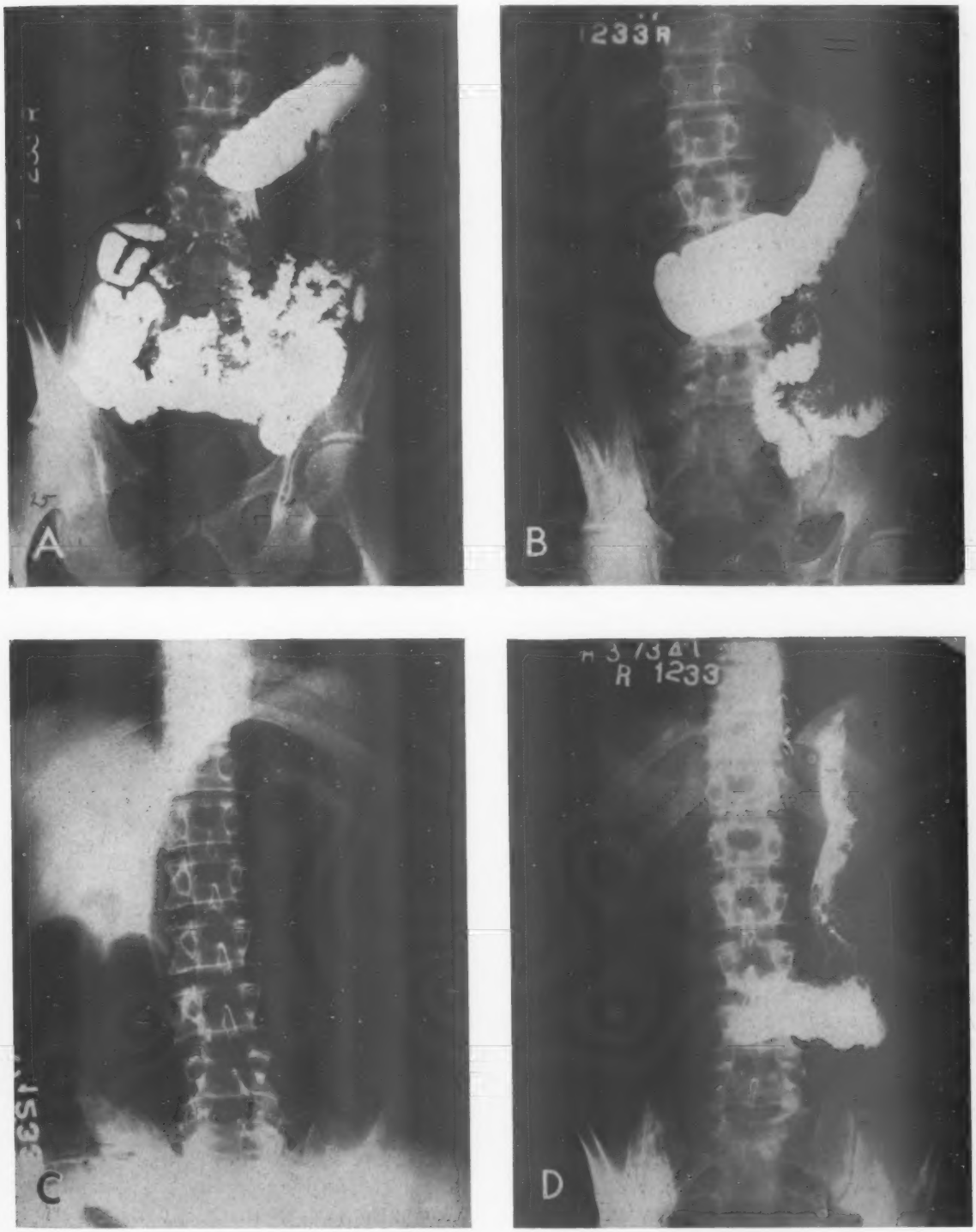

FIG. 6. Same patient with severe gastric hypotonicity for two and a half months with persistent ulcer. (*A*) Pre-vagotomy, crater. (*B*) Two weeks post-vagotomy, ulcer almost healed. (*C*) Three weeks post-vagotomy, sudden severe gastric hypotonicity. (*D*) Two and a half months post-vagotomy, persistence of severe gastric hypotonicity.

The preoperative twelve hour overnight volume of free hydrochloric acid dropped immediately after vagotomy from 44 to 23 units.

During the next two years, both of these values rose toward the normal base line,* although neither of them reached the normal volume of gastric secretion or the normal units of hydrochloric acid content.

Effect of Vagotomy on Small Intestine. Ten cases were selected for serial studies of the small intestine (with barium and water mixture) at intervals of one-half hour, at two weeks, and at one, three, six and twelve months after vagotomy. In many other cases studied, additional films were taken at seven, eight, ten and twenty-four hours. All gastrointestinal roentgenograms were checked for changes in the small intestine. Table VI illustrates these findings.

In general, the majority of the patients in this series developed mucosal coarsening and segmentation of the small intestine as well as a mild to moderate degree of delayed progression. This delayed progression subsided six to twelve months after vagotomy (Fig. 7).

Effect of Vagotomy of Other Intra-abdominal Organs. During the routine post-vagotomy gastrointestinal examination, the esophagus was studied with each patient in the upright position. For completeness, in 8 cases, the esophagus was studied with patient in the horizontal position. No alterations of normal size, of normal peristalsis, or of the normal progression of barium was observed in the esophagus.

* Normal base line or level that is found in patients without peptic ulcer.

Oral cholecystographies performed before vagotomy were compared with those taken at intervals of two weeks to three months after vagotomy in 7 patients. In all these patients, the gallbladder was normal in size, concentrated radiopaque solution well and emptied readily after a fatty meal.

In order to evaluate the post-vagotomy colon changes, 3 types of roentgenographic examinations were used: the six hour films of every gastrointestinal series, serial films taken at intervals of seven to twenty-four hours after ingestion of barium, and films of barium enemas performed at intervals of two weeks to six months after vagotomy in 5 patients. In the majority of all patients, the progression of barium, haustra and lumen size of the colon were normal.

Table VI

VAGOTOMY EFFECTS ON SMALL INTESTINE

Time	Segmentation and Coarsening of Mucosa	Delayed Progression to Cecum	Dilated Loops of Small Intestine	Insufficient Barium	Normal
1 mo.	39	30	0	4	5
3 mo.	21	14	0	0	18
6 mo.	19	10	0	0	18
1 yr.	3	0	0	0	34

Colon irritability distal to Cannon's point and accelerated progression of barium were found in the few patients who had transient diarrhea. Coincidentally and a short time later, these alterations within the colon and the diarrhea subsided. The proximal third of the colon was always found to be normal.

Intravenous pyelograms taken before vagotomy were compared with similar studies made from two weeks to three months after vagotomy in 5 patients. No abnormal changes in the urinary tract were observed.

SUMMARY

Since this series is small (47 patients) and the time of follow-up examinations is relatively short, no undisputed conclusions

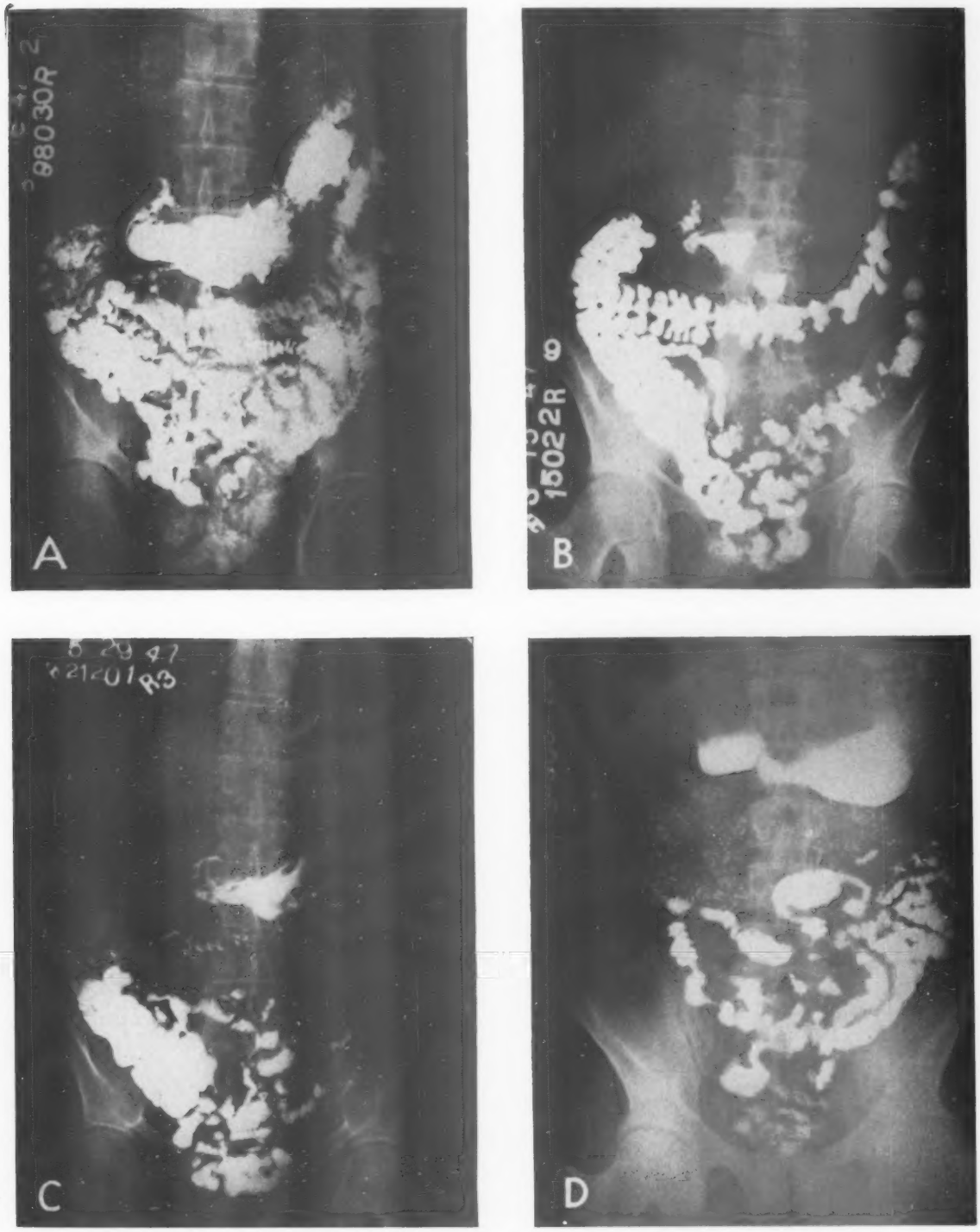

Fig. 7. Small intestine changes following vagotomy. (*A*) Case I. Two hour film one month post-vagotomy. (*B*) Case II. Six hour film two months post-vagotomy. (*C*) Case III. Three hour film six months post-vagotomy. (*D*) Case IV. Six hour film six months post-vagotomy.

concerning the clinical effect of vagotomy upon peptic ulcers can be drawn. It is my opinion, however, that treatment of peptic ulcers by vagotomy without concomitant gastroenterostomy is not superior to other methods of treatment for peptic ulcer.

Following vagotomy, no abnormal roentgenographic changes were observed in the esophagus, in the gallbladder or in the urinary tract of some of the patients in this series. In the majority of these patients, the colon failed to show abnormal changes, although in a few of them, irritability and hypermotility occurred concomitantly with a transient diarrhea.

During the first postoperative year, the majority of patients in this series showed changes in the mucosa of the small intestine with a mild to moderate degree of hypermotility of that subdivision of the gastrointestinal tract.

Gastric atony was the most common postoperative result of vagotomy in this series. Five of these patients had persistent peptic ulcers. Four of the five required partial gastrectomy and the remaining one, a gastroenterostomy for relief of severe atony of the stomach.

Vagotomy in man does achieve the two conditions which are postulated by Dragstedt as essential for the healing of peptic ulcers and for the prevention of their recurrence, namely decreased gastric secretion and motility. Nevertheless, in this series of forty-seven patients, peptic ulcers in the duodenum or in the jejunum persisted for one month in fourteen patients, for two months in eleven patients, for three months in eight patients, for six months in four patients, for one year in three patients and for two years in the remaining one.

Of the forty-seven patients who underwent vagotomy, ten had peptic ulcers which recurred from ten to twenty-seven months after their operation.

I wish to express my sincere appreciation to Dr. Ross Golden for his advice, suggestions, and guidance in the writing of this paper.

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DISCUSSION

DR. ROSS GOLDEN, New York, N. Y. The clinical indications for and the clinical results of vagotomy are under dispute, as is brought out by Dr. Priviteri's excellent presentation.

At the Presbyterian Hospital in New York very few vagotomies have been done. The results from partial gastrectomy for intractable peptic ulcer, in the hands of our surgeons, have been so good that they are not inclined to use vagotomy.

One of the interesting sidelights from this and other similar studies is the physiologic change which occurs in the stomach following the section of the vagus nerves. More than twenty years ago Dr. Klein, working under the direction of Dr. Allen O. Whipple in the surgical laboratory of the College of Physicians and Surgeons, found that when he sectioned the vagus nerves in dogs peristalsis was greatly reduced or obliterated for a time, and that the stomach later regained its motor power. We have been taught that the parasympathetic furnishes the motor influence on the stomach and that it exercises a relaxing effect on the pylorus. The role of the sympathetic is supposed to be the reverse. Presumably it counteracts the motor influence of the parasympathetic on the stomach but has a motor influence on the pylorus. It is apparent that in these post-vagotomy cases, not only by the roentgen ray as shown by Dr. Priviteri, but also by gastroscopy, the pylorus is wide open and the delay in the emptying of the stomach cannot be attributed to pyloric obstruction. Consequently it would appear that at the same time that the parasympathetic influence is reduced, the influence, whatever it is that causes a contraction of the pylorus, is also reduced. This appears to be at first glance a contradiction of what we have been taught for many years. In this connection it is interesting that physiologists now recognize the presence of adrenergic fibers in the parasympathetic and cholinergic fibers in the sympathetic. It is therefore possible that sectioning of the vagus interrupts an adrenergic influence on the pylorus which is ordinarily attributed to the sympathetic.

Later in most human cases, as in the dog experiments, the stomach recovers its motor power. The presumed explanation is that the intramural nervous system of the stomach can take over and furnish enough parasympathetic influence so that peristalsis will again be effective. It would appear that this process of taking over can be accomplished more readily in some stomachs than in others. This aspect deserves further investigation.

Dr. Priviteri should be complimented on the excellence of this presentation.

DR. PRIVITERI (closing). Thank you very much Dr. Golden. I just want to emphasize that as far as this series is concerned, the findings may only be consistent with this type of procedure—a vagotomy without gastroenterostomy. Most of the work on vagotomy has been done with associated gastroenterostomy.

I think that vagotomy offers a rather unusual opportunity to study the physiology of the gastrointestinal tract and we should avail ourselves of it. Vagotomy has expelled from our minds the fear of vagus nerve injury. You remember that in 1946 everyone was concerned about the effects of vagotomy on other intra-abdominal organs. The Mount Sinai Group in New York feared intra-abdominal complications after vagotomy. I think that as a result of vagotomy, these problems have been dispelled very well.

Vol. 65, No. 4

THE SIGNIFICANCE OF OPAQUE MEDICATIONS IN THE GASTROINTESTINAL TRACT, WITH SPECIAL REFERENCE TO ENTERIC COATED PILLS

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RADIOLOGISTS are only too familiar with the frequent finding of opaque pills in the gastrointestinal tract. Such opacities are a constant source of annoyance to radiologists the world over. As a rule, the radiologist exerts considerable effort to have the patient properly prepared for the examination of the abdomen, such preparation including catharsis, cleansing enemas, pitressin, etc. After such preparation, it is with irritation that he finds on the film one or more opaque pills projected through the kidneys, ureters, bladder or gallbladder (Fig. 1, 2 and 3).

Many patients will faithfully follow instructions for preparation before an abdominal or urological examination, and will dehydrate, fast and purge themselves. They also follow the instructions of their family physician and continue to take their usual pills as directed. Even in hospital roentgenological practice where patients are properly "prepared," there is a surprisingly high incidence of medicinal opacities of this type. As a rule, a "plain film of the abdomen" or so-called "KUB" film is requested in order to rule out the possibility of opaque calculi. In such cases the presence of opaque medication in pill form is particularly unfortunate. To be sure one can

Fig. 1. Plain film of abdomen. The enteric coated pill in the lower gastrointestinal tract simulates a ureteral calculus.

Fig. 2. Unusually large semi-opaque pill projected through the right upper quadrant simulates a biliary calculus.

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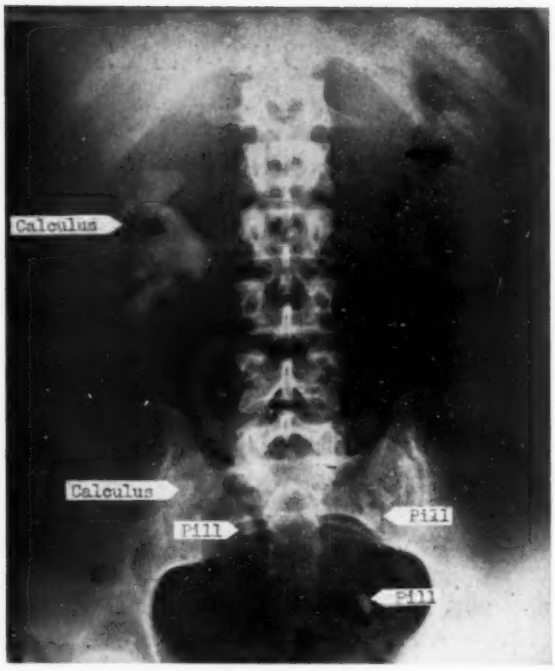

Fig. 3. Plain film of abdomen reveals an assortment of opacities including renal calculi; a ureteral calculus and three enteric coated ammonium chloride pills. Identification of the various opacities was accomplished on subsequent excretory and retrograde studies.

develop the film, study it, and then obtain oblique or lateral complementary films as indicated. Roentgenoscopy with palpation is also practicable. However it is much more convenient to obtain a satisfactorily diagnostic film in the first place.

The undesirability of opaque medication in the gastrointestinal tract, especially in pill form, is so well appreciated by radiologists, that it is unnecessary to dwell upon this phase. It is the purpose of this paper to point out another aspect of the situation; namely, that the finding of such medication in the lower small intestine, ileocecal region or colon, is significant to the referring physician and to the patient. If opaque pills are found in these locations, the medication is not dissolved, and if not dissolved, cannot be expected to exert proper therapeutic effect. In such an instance, the radiologist can render the referring physician a service by informing him that the medication he is using is passing through the gastrointestinal tract unchanged. As a rule, this will come as a surprise to the physician, and he will be glad to change the medication in order to obtain the therapeutic effect for which he is striving.

As an example of the value of such observations by the radiologist, I shall set forth briefly an incident which occurred in our hospital. As is the case on most urological services, there is a very definite indication for changing the reaction of the urine from alkaline to acid. Most patients with urinary infections have alkaline urines, and modern treatment frequently consists of the administration of urotropin or mandelamine which must act in an acid medium. The acidity in the former case is usually attained through the use of enteric coated ammonium chloride.

Our urological service for more than a year administered enteric coated ammonium chloride in sufficient quantities, but three highly undesirable effects were observed:

1. Urinary reactions continued to be alkaline.
2. Urinary antiseptics were ineffectual.
3. Roentgen examinations were constantly hampered because of the presence of opaque pills in the small intestine and colon.

In this particular case we found that the enteric coated ammonium chloride had been bought in a large lot (for economic reasons) and had been stored for more than a year. Tests showed that the coating had become undesirably insoluble. Undissolved enteric coated ammonium chloride pills were recovered from the feces of patients receiving such medication, and following the completion of the simple solubility tests described below, the old, dehydrated, insoluble pills were discarded.

The urological service is now using the "new type" ammonium chloride and since this preparation has been employed, all three undesirable effects have been obviated. Urine showed a prompt reversal to the acid side, infections responded satis-

factorily to treatment and we no longer see opaque pills in the gastrointestinal tract in the Department of Radiology. The clinicians were extremely grateful to us for the discovery of the insolubility of the medication.

It is common for physicians in general practice to purchase and store their medications, dispensing them as indicated. We have seen extreme examples of insolubility result from this practice. Figure 4 shows innumerable opaque pills in the cecum of a patient who was being treated for diarrhea by her family physician. The medication in this case was identified as bismuth subcarbonate which, while not enteric coated, was obviously insoluble.

Medication will pass unchanged through the gastrointestinal tract if the pill or capsule is too resistant to the digestive enzymes encountered or if there is deficient enzymatic activity. We have seen examples of both of the above. Enteric coated pills are by far the greatest offenders, These are usually prepared in such a way that they will not dissolve in the acid medium of the stomach and are given a protective coating which is more or less insoluble in digestive juices. Certain coatings are unsuitably made, or become increasingly insoluble with age. Such preparations pass unchanged through the gastrointestinal tract and may be recovered from the stools.

The dissolution of any enteric coated pill, and also of certain other hard pills is dependent upon the enzymic action of the digestive juices, the pH of the environment, and the agitation induced by peristalsis. Any or all of these variable factors may be deficient. This is a relative matter, as can be illustrated by the fact that we have come in contact with a certain variety of enteric coated ammonium chloride pill which almost invariably passed intact through the intestinal tract of elderly debilitated bed patients in the hospital, yet was almost always dissolved in the small intestine of young healthy persons. This is, in our opinion, evidence of deficient digestive action on the part of the group of elderly patients,

Fig. 4. Cholecystogram. An incidental finding is the presence of many undissolved bismuth subcarbonate pills in the gastrointestinal tract. An unusually large group is in the cecum (arrow).

all of whom were over seventy. We did not determine gastric acidity or attempt any quantitative or qualitative evaluation of small intestinal enzymes.*

ENTERIC COATED MEDICATIONS

Most physicians know very little about enteric coated pills, capsules, etc., as factual information dealing with such matters is usually to be found only in texts and periodicals written and read by those pharmaceutically inclined. It is rare to find articles on this subject in medical journals. For this reason it may not be amiss to comment briefly on the subject.

I obtained some background from standard pharmaceutical texts, and wrote letters of inquiry to several of the leading pharmaceutical firms in the country. All of

* In some of the above experiments, hospital interns were used. These young men repeatedly demonstrated their superiority in pill digestion, and, with three exceptions, we found no pills which would pass unchanged through their intestinal tracts. Not only were the interns incomparably better than elderly bed patients, but they were also appreciably superior to young individuals of both sexes hospitalized for lower abdominal surgical procedures.

these have been very cooperative. The general tenor of the letters received in reply to our inquiries is such as to reflect credit upon our research-minded pharmaceutical houses.

The facts gathered may be summarized as follows: There is no generally accepted method for the preparation of enteric coated medications. As the name implies, such preparations are expected to pass through the stomach intact, but to disintegrate rapidly in the small intestine. This, it appears, is not readily accomplished. Practically every firm has its own process, many of which are secret for obvious reasons.

In general, the steps involved in the preparation of so-called enteric coated pills or capsules are as follows:

1. The active ingredient is formed into a pill which is given a "size coat" in a revolving metal coating pan. This coat is similar to confectioner's glaze and often contains shellac. It acts as an undercoat for the heavier enteric coatings and prevents permeation of subsequent coatings into the active ingredient.

2. Enteric coating (consisting of whatever the manufacturer prefers to use) is applied in the form of a fluid while the pills are agitated in the coating pan. After each coat of this special material is applied, the pill is dried, and the process is repeated. Some companies using a form of confectioner's glaze apply five to eight coats. Others using cellulose preparations apply as many as sixty coatings.[20] The nature and number of coatings are extremely variable.

3. A finish coating consisting of sugar and coloring matter is applied. This coating is usually soluble in water and supplies flavor and pharmaceutical elegance.

Enteric coatings have been used since 1844 when Unna brought out a protective coating composed of keratin.[13] Since that time, a great many substances have been used, and a great deal of research has been directed and is still being directed toward further improvement in methods.

Among the substances used in this connection may be mentioned:

Formalin-gelatin
Stearic acid
Ammoniated white shellac
Salol, alone and in combination
Cetyl alcohol and mastic
Various cellulose acetates
Celteric
Rosin
Cellulose acetate phthalate
Shellac and castor oil
Hydrogenated fats
Tragacanth, elm bark, carnauba wax and sugar
Combinations of the above

In addition to the above, there are a series of more modern preparations which cannot well be discussed because of "trade secrecy." Most companies have gone to a great deal of effort and expense to develop new and more satisfactory combinations and synthetic preparations. It is generally agreed that the modern substances are superior to those previously used, but it is still possible to purchase enteric coatings of the older type which are made by less progressive concerns, or which are old, stale and dehydrated. The fact that these inferior preparations still find a market reflects upon the medical profession which is actually the consumer.

STANDARDIZATION AND TESTING OF ENTERIC COATINGS

At the time of this writing, there is no national standardization of specifications for enteric coatings, although this will no doubt come to pass.* There is, furthermore, no standard method of testing the solubility of preparations placed upon the market by the manufacturers of such products. Most reliable pharmaceutical companies use several methods to test the solubility of their enteric coatings. These tests are usually carried out in vivo and in vitro. In the former, barium pills are made and coated as described above. After ingestion, the progress and dissolution of the pills is

* A national committee of the ADMA-APMA with Mr. Elmer B. Vliet of the Abbott Laboratories as chairman is engaged in standardizing testing equipment for enteric coatings as well as determining definite specifications of solubility which shall be met by manufacturers of such pharmaceutical products before release for consumption.[19]

followed by serial roentgenograms.[5,13,14] A modern trend in such testing is exemplified by the method of enteric coating one of the radioactive salts. When the coating is permeated, the radioactive salt can be readily detected in the circulating blood.[8,20]

In vitro tests are more or less conventional and are based upon solubility studies carried out in an acid medium and subsequently in an alkaline medium at body temperature. The refinement of constant mechanical agitation is usually added.[10,13,14] Such testing, of course, is designed to evaluate a coating which resists acid but dissolves in an alkaline environment.

An acid medium commonly used (artificial gastric juice) consists of:

Pepsin N.F.	3.2 gm.
HCl U.S.P.	2.5 cc.
NaCl U.S.P.	2.0 gm.
Distilled water	1,000 cc.

Various other acid solutions are used,[5,7] some investigators adding potassium and calcium salts, etc. As a rule, this solution has a pH of about 1.6. A good enteric coating is expected to tolerate this acid medium without change for at least an hour. Some manufacturers require the preparation to withstand this artificial gastric juice for several hours. Resistance to an alkaline medium is subsequently tested in a similar manner.

Artificial Intestinal Fluid

Pancreatin	U.S.P.	2.8 gm.
Sodium bicarbonate		15 gm.
Distilled water	q.s.ad.	1,000 cc.

The pH of this solution is about 8.0 or 8.5.

It is customary to adjust the enteric coating so that it will become permeable or will disintegrate entirely in this solution. Here, again, there is no general agreement as to time, for some manufacturers recommend coatings which break up in a very few minutes,[17] while others prefer a time of one or two hours. Some of the enteric coated pills we have tested have failed to disintegrate in twenty-four hours. We appreciate that these may have changed in regard to solubility between the time of their manufacture and their exposure to our test solutions.

Laboratory methods of testing enteric coatings for solubility do not always agree closely with clinical tests. This is in part due to the fact that for years workers labored under the misapprehension that the stomach was strongly acid and the intestinal tract was alkaline. This can no longer be credited, as many workers have shown that the gastric pH is often on the alkaline side due to reflux of pancreatic juice.[2] It is well known that the incidence of gastric achlorhydria is directly proportional to the age of the patient,[12] so that stomach contents are by no means always acid.

Bile and pancreatic juice are slightly alkaline fluids, and one might expect the small intestinal contents to be alkaline. Bollman and Mann,[3] however, working with dogs, found that during digestion the pH in the duodenum varied between 3.8 and 6.6. The entire jejunum was definitely on the acid side of neutral. Physiologists[1] state that the intestinal contents as far down as the ileocecal valve are frequently acid.

It follows, of course, that an enteric coating designed to dissolve in artificial intestinal fluid having a pH of 8.5 will not by any means dissolve in a slightly acid or very weakly alkaline small intestine. Certain pharmaceutical research departments have modified their testing procedures and their laboratory testing fluids to simulate those encountered in the human small intestine. Others continue to put preparations on the market which will not dissolve for many hours in strong acids or alkalis.

One company[13] has now discarded the conventional acid-followed-by-alkaline testing technique and depends entirely upon time, temperature and moisture without regard to pH. The coating used in this instance consists of agar, elm bark, stearic acid and carnauba wax.*

The greatest variable in solubility prob-

* We have had occasion to test this preparation and have found it very satisfactory. We have also tested other modern enteric coatings with similarly satisfactory results. The author has no wish to recommend the products of one manufacturer over those of others.

lems is the one which cannot be standardized; namely, the patient. Gastric and intestinal juices in elderly individuals are unpredictable and variable. Achlorhydria is common, gastric emptying is slow, peristalsis is irregular and ineffectual, and pancreatic juice and bile are less plentiful and less powerful. For these reasons the in vivo tests of insolubility remain the most clinically accurate. The simplest method for such evaluation is daily within the grasp of all radiologists who see films of the abdomen.

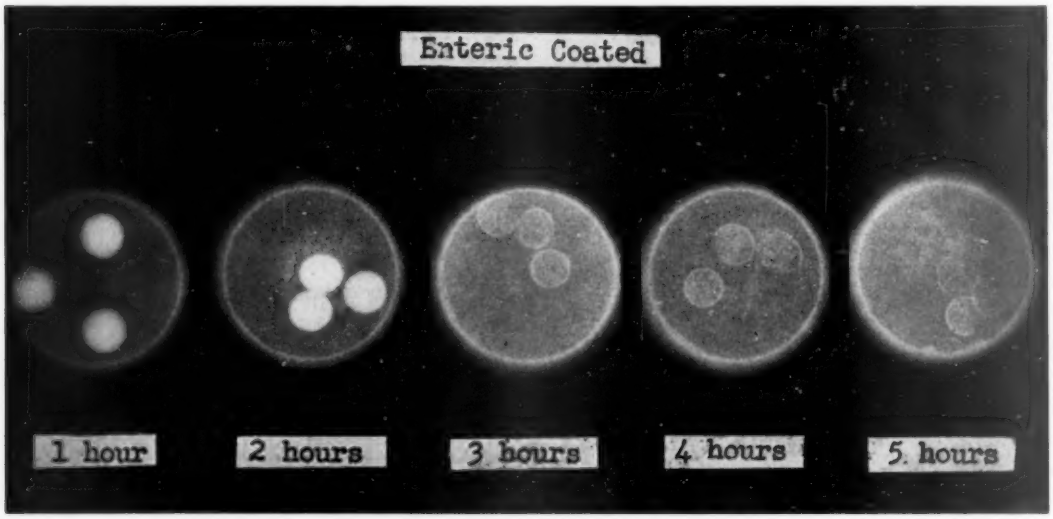

Fig. 5. Roentgenological demonstration of clinically acceptable enteric coated ammonium chloride pills dissolving in 1/10 normal sodium hydroxide at body temperature. At three hours the coating has been penetrated and the active ingredient is going into solution even though the enteric shells retain their outlines. At five hours only fragments of the enteric coatings remain. (Roentgenograms were made in paper cups without removing the pills from the sodium hydroxide solution.)

SIMPLE GROSS SOLUBILITY TEST (IN VITRO)

In the course of preparation of this work we have carried out many simple solubility tests using enteric coated medications made by several pharmaceutical houses and purchased from or donated by drug stores in the general vicinity of Danville.

We find that without elaborate testing equipment it is possible to approximate the degree of solubility of these preparations by merely placing them in 1/10 normal (4 gm. per 1,000 cc.) sodium hydroxide in the bacteriological incubator and agitating them every hour. In our experience, pills which dissolve in less than four hours are suitable for clinical use as judged by control in vivo tests.*

This method of gross testing of solubility is much less accurate and less reliable than the proper pharmaceutical testing procedures followed by modern drug houses, but it is easily performed and in our experience has served as an approximate practical guide to comparative solubility.

Satisfactory solubility in 1/10 normal sodium hydroxide at 37° C. is demonstrated roentgenologically in Figure 5. It is not necessary to obtain such roentgenograms, as visual inspection is usually adequate.

SUMMARY

The presence of intact pills, capsules and tablets in the lower small intestine and large intestine is more than a nuisance to

* In carrying out this simple test it is wise to first wash the pills in water to remove the colored sugar coating and to inspect them carefully each hour for penetration of the enteric layer. If the sodium hydroxide becomes turbid it may be replaced with fresh solution.

the radiologist. It is clinically significant. Absence of desired therapeutic effect can often be traced to failure of dissolution of the medication.

Pills may remain undissolved because of inherent insolubility of the medication or deficient dissolving power on the part of the patient.

Simple solubility tests can be conducted quickly and economically on any medications suspected of undesirable insolubility.

Many "old style" enteric coated preparations contain substances which withstand the action of digestive enzymes. These are inexpensive but of no value, and should be discarded.

Certain enteric coatings, especially those of the formaldehyde-treated gelatin, rosin and shellac, become progressively more impermeable with aging and dehydration. Such preparations should not be stored for long periods of time.

Elderly and chronically ill patients evidence inability to dissolve certain enteric coatings which are adequately handled by young healthy individuals. If such patients require enteric coated medications, a coating should be selected which is readily dissolved.

Radiologists should direct the attention of referring physicians to the presence of undissolved pills in the small intestine and colon, and should point out the implications of such a finding.

Clinicians should evince critical interest in enteric coated preparations in order that they may avoid the use of insoluble preparations which are therapeutically worthless.

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THE ANTERIOR TUBERCLE OF THE FIRST CERVICAL VERTEBRA AND THE HYOID BONE: THEIR OCCURRENCE IN NEWBORN INFANTS*

By ARTHUR C. TOMPSETT, Jr., M.D., *and* S. W. DONALDSON, M.D.
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THE ossified anterior tubercle of the first cervical vertebra and the ossified hyoid bone are often seen in the lateral roentgenogram of the infant neck. No reference is found in the roentgenologic literature concerning their incidence at birth. However, Hill[2] in his anatomic study of 500 fetuses found that the center for the body of the hyoid was present in 59 per cent of newborns and appeared as early as the fifth fetal month in some cases. This paper is an attempt to establish this incidence as seen roentgenologically and to point out the possibility of misinterpretation of these structures in the newborn.

The films of 500 consecutive newborn infants were studied. In this hospital all newborns have routine roentgenograms for thymic enlargement. The lateral film is taken to include the base of the skull and shows the cervical structures. This examination is usually made within five days and the first or second day after birth. The occasional premature infant is not examined until no harm will come from the trip to the department of roentgenology. There were slightly more males than females in the 500 selected cases and, in order to make equal groups, several additional females were tabulated and a like number of males dropped from the study. This, then, made 250 of each sex. No consideration was given to prematurity, weight or size since in a group of this size such variables would be of no importance. Race was not noted since only 3 to 4 per cent of the total births in this hospital are of the colored race.

ANTERIOR TUBERCLE OF THE FIRST CERVICAL VERTEBRA

The first cervical vertebra, or atlas, is ring shaped and has no body. The part which in other vertebrae would become the body is instead fused with the body of the axis to become the odontoid process. The atlas then consists of two lateral masses connected by a short anterior arch and a longer posterior arch.[6] It is formed from three main centers of ossification: one for each lateral mass which also extends to form the posterior arch, and a third center in the anterior arch which is commonly called the anterior tubercle. The two lateral masses are seen on the roentgenogram at birth and unite posteriorly in the fourth to fifth year.[7] The center in the anterior arch is said by Piersol[6] to be found in the course of the first year. Hodges[3] gives the average time of appearance at eleven months, and Camp[1] gives it at one year. No mention was found of its occurrence at birth.

Many anomalies of the atlas occur. Lack of anterior arch, failure of closure of posterior arch, double anterior nucleus, median suture in the anterior arch, and other abnormalities have been reported[5,6,7] which might be of importance from a medicolegal or compensation viewpoint.

In the lateral roentgenogram of the cervical spine in the newborn, the ossified anterior tubercle is seen as a roughly triangular or rectangular area of bony density lying anterior and superior to the lateral masses of the first cervical vertebra which are superimposed upon each other (Fig. 1). It is directly below the ring-like tympanic portion of the temporal bone. In the cases studied it varied in size from a diameter of 4 millimeters to the smallest area which could be identified.

In this study, the anterior tubercle was seen in 103 of the 500 infants examined,

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or 20.6 per cent. There was no appreciable difference in the sexes as it was seen in 54 of the 250 males, or 21.6 per cent, and in 49 of the females, or 19.6 per cent (Table 1).

TABLE I

INCIDENCE OF OCCURRENCE OF OSSIFICATION IN THE ANTERIOR TUBERCLE OF THE FIRST CERVICAL VERTEBRA AND THE HYOID BONE AT BIRTH

	Cervical Vertebra	Hyoid Bone
Males (250)	54 (21.6%)	188 (75.2%)
Females (250)	49 (19.6%)	188 (75.2%)
Totals (500)	103 (20.6%)	376 (75.2%)

In any roentgenogram of the cervical region for consideration of fracture, dislocation, foreign body, developmental defects, etc., the occurrence of this structure must be borne in mind. With slight extension or rotation of the neck, and even with the neck straight, its location is considerably different than the position which might be thought to be normal by the observer.

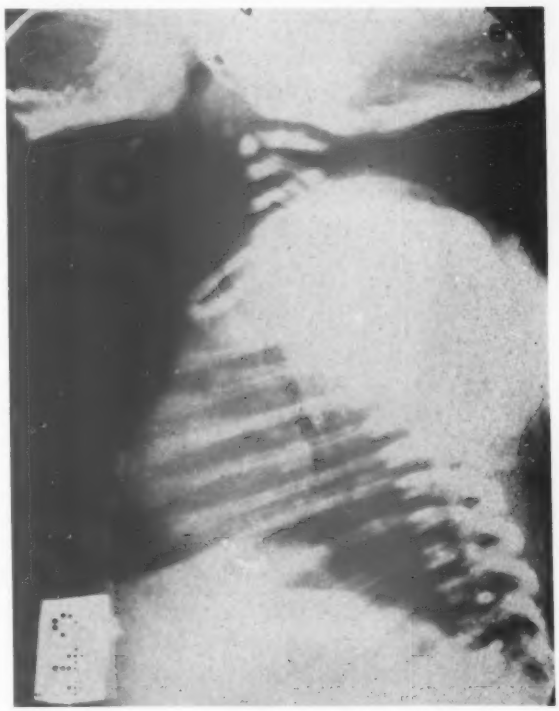

FIG. 1. Lateral roentgenogram showing the anterior tubercle of the first cervical vertebra below the ring-like tympanic portion of the temporal bone and the hyoid bone below the mandible.

THE HYOID BONE

The hyoid bone originates embryologically from the second and third branchial arches. It consists of the body and a pair of lesser and greater horns. Piersol[6] states (from Sutton) that anatomically two nuclei appear in the body in the fourth fetal month. The time of appearance of ossification in the lesser horn varies from a few months to adolescence. Köhler[4] states concerning the hyoid: "It is usually visible in the first few years of life, its body at any rate" . . . "Cornua appear between the sixth and tenth years." The three charts in common use, showing the development of the skeleton[1,3,4] do not mention the time of appearance of the hyoid. No reference was found of its incidence at birth.

In the lateral roentgenogram of the newborn, the ossified body of the hyoid is seen as a triangular area of bony density and the greater horns appear as slightly curved lines extending posterior from the body. They lie well anterior and just below the mandible (Fig. 1).

The hyoid was recorded as visualized if either the body or horns were seen. Most commonly only the body was present. In the 500 cases in this group the hyoid was seen in 376, or 75.2 per cent (Table 1). Exactly the same incidence was found in males as in females.

The hyoid, as is shown, occurs much more commonly than the anterior tubercle of the first cervical vertebra but it also is not always visualized at birth as is commonly believed. It also may be confused, particularly with opaque foreign bodies, and should be kept in mind in interpretation of films of the infant neck.

As an incidental finding in 11 of the 500 cases, the anterior tubercle of the first cervical vertebra was seen when the hyoid bone was not. This is the reverse of the usual finding, as is seen in Table 1. The significance is not known.

SUMMARY

1. The lateral cervical roentgenograms of five hundred newborn infants were studied.

2. The anterior tubercle of the first cervical vertebra was ossified in 20.6 per cent.

3. The hyoid bone was ossified in 75.2 per cent.

4. The location of these structures is described and attention called to the possibility of misinterpretation.

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MULTIPLE MYELOMA COMPLICATING PAGET'S DISEASE*

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ALTHOUGH Paget's disease is a fairly common entity and multiple myeloma not rare, coexistence of these lesions is apparently very unusual. In a recent article Adams *et al.*[1] point out that in the differential diagnosis of multiple myeloma, certain bone diseases including Paget's disease must be considered. He states that "one factor in the diagnosis of multiple myeloma is the occurrence of abnormality of plasma proteins. It is also aided materially by a careful study of the serum calcium and inorganic phosphorus levels and a determination of the alkaline and acid phosphatase activity. When this information is added to careful roentgenographic interpretation, much confusion may be averted." Reich and Brodsky[5] described one case in 1948 and mentioned that the only other case of this type they were able to trace was through a personal communication from Snapper. We were able to find in the literature only one other case with satisfactory pathological study.[6] Williams,[9] in a letter to the "Lancet" in 1909, stated that "the neoplastic disease most commonly associated with osteitis deformans was multiple myeloma," but he failed to quote any confirmatory pathological studies and from the paucity of subsequent reports, his statement has not been substantiated. Sear[7] states, "I have seen Paget's disease complicated by prostatic secondaries, and I have seen multiple myeloma in association with Paget's disease. Paget's disease and multiple myeloma occur at much the same age period, and it will be interesting to see if in the future more such cases are noted, especially as more cases of multiple myeloma are now being recognized; or possibly that lesion is on the increase." It is the purpose of this communication to report a third case of multiple myeloma complicating Paget's disease in which roentgenographic and histopathologic studies were made.

CASE REPORT

L. H. B., a white male, aged sixty-seven, was admitted to the hospital on October 19, 1946, with a complaint of pain and redness of the left foot. On admission, physical examination disclosed that the area of involvement and complaint was limited to the left lower extremity. A dime-sized area of redness and swelling was observed on the mid-dorsal surface of the left foot, which became black and necrotic approximately one week after admission. Soon afterward the entire dorsum of the foot showed similar changes and a diagnosis of arteriosclerotic gangrene was made. A routine roentgen study on October 23, 1946, showed extensive changes in the femora and tibiae characteristic of Paget's disease. The history revealed that a diagnosis of Paget's disease had been made on this patient in 1938. At that time he suffered a pathologic fracture of the left femur which healed in deformity.

On admission roentgenograms of the skull (Fig. 1 and 2), thorax and spine revealed evidence of extensive Paget's disease. The blood count was essentially normal with a white count of 7,500 and normal differential; the red blood cell count was 3,840,000 with 13.2 gm. of hemoglobin. A serum alkaline phosphatase showed 15 units (King-Armstrong). The test for Bence-Jones protein in the urine was negative.

On February 20, 1947, an amputation

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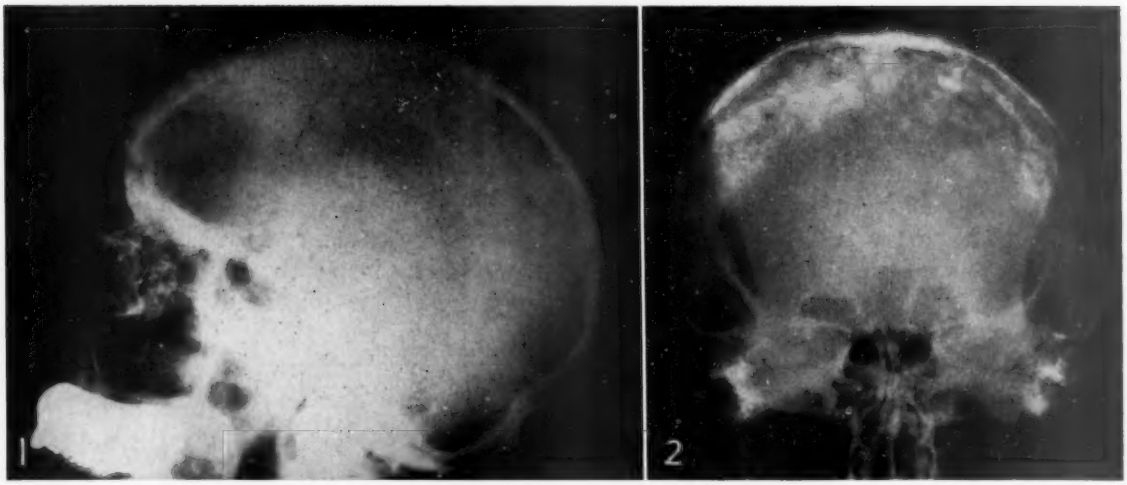

Fig. 1 and 2. Skull films on admission, showing the typical changes of Paget's disease. An interesting finding was the symmetrical areas of osteoporosis circumscripta.

through the middle of the left thigh was performed. Pathological examination of the leg revealed marked sclerosis of the arteries with narrowing and eccentricity of the lumen. Histologic sections showed almost complete occlusion of one of the vessels by a thrombus. Pathological diagnosis was arteriosclerotic gangrene. After the amputation convalescence was uneventful. The patient remained comfortable except for occasional complaints of pain in the right shoulder and in the back. On November 16, 1947, he developed a temperature of 103° F. Examination of the chest revealed diffuse rales throughout the lung fields. The blood nonprotein nitrogen rose to 38.5 mg. per 100 cc. He was treated with antibiotics and intravenous fluids with some temporary improvement. On November 18, 1947, examination of the heart revealed a tachycardia of 130 beats per minute with an irregular rhythm. An emergency electrocardiogram showed a typical Q-I T-I pattern compatible with myocardial disease. The patient's condition became increasingly poor and he died on November 24, 1947.

A postmortem examination was performed. On sawing through the skull cap numerous soft, hemorrhagic growths were visible on the internal surface (Fig. 3). These varied in size from 1 to 3 cm. in diameter with no evidence of reaction in the adjacent portions of the skull, meninges, or brain. The skull cap was sent to the

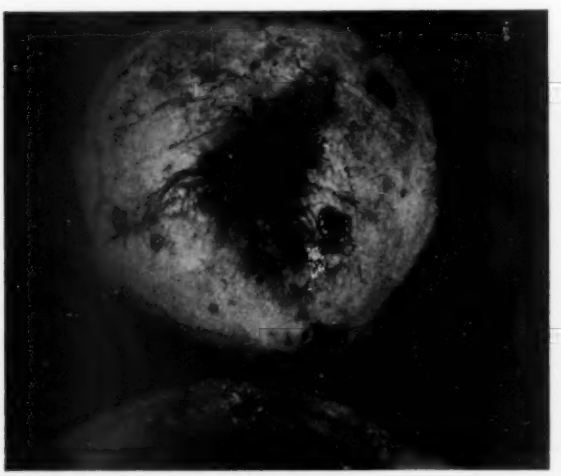

Fig. 3. Portion of the calvarium with numerous hemorrhagic tumors on inner surface, measuring 1 to 3 cm. in diameter.

Fig. 4. Roentgenogram of calvarium specimen shown in figure 3.

roentgen department for study and films revealed numerous punched-out areas scattered throughout the calvarium, which itself was extensively altered by the typical changes of Paget's disease (Fig. 4). The ribs cut easily and

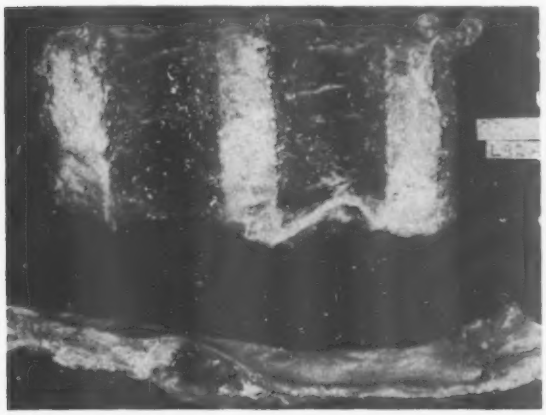

Fig. 5. Vertebrae and rib showing extensive replacement by hemorrhagic tumor tissue.

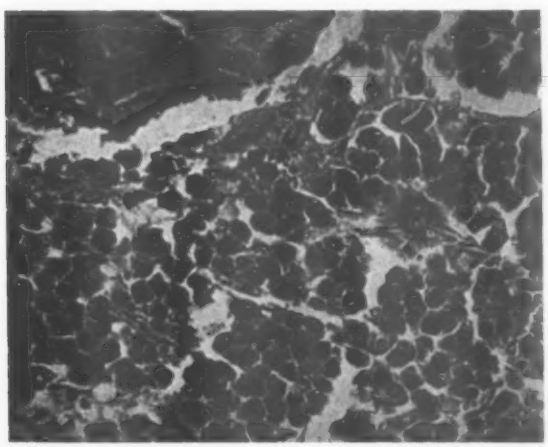

Fig. 6. Myeloma in skull. The cells here are characterized by large nuclei with clumping of chromatin.

were more fragile than normal; the fifth left rib in the axillary line contained a large mass of tumor tissue consisting of a soft, hemorrhagic growth. Similar tumor tissue was seen throughout the marrow in the remaining ribs and nodular accumulations were seen at the surface of some of the ribs. The marrow of the sternum and the vertebrae (Fig. 5) were similarly extensively replaced by soft, hemorrhagic tissue. Microscopic study of the bones of the skull, ribs and vertebrae (Fig. 6–10) showed marked coarsening of the trabecular pattern, with irreg-

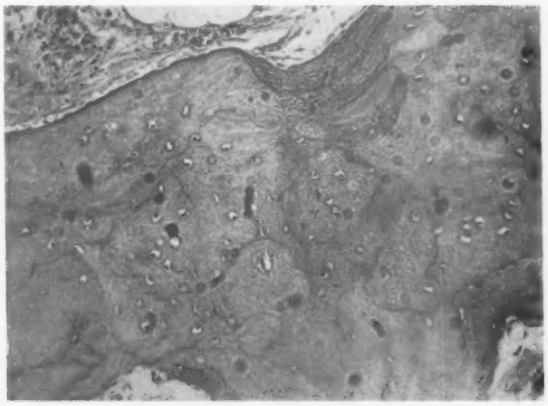

Fig. 7. Skull showing "mosaic" pattern and prominent cement lines of Paget's disease.

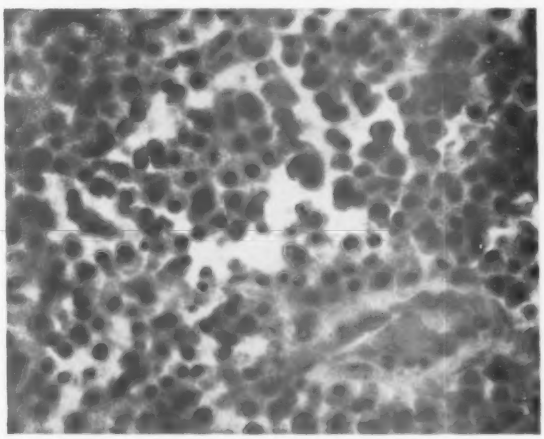

Fig. 8. Adjacent areas of myeloma and Paget's disease in skull.

Fig. 9. Myeloma in body of vertebra. Here the cells are smaller and the nuclei more pyknotic.

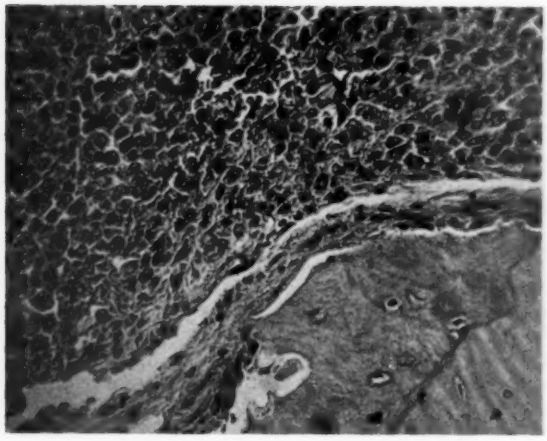

Fig. 10. Rib showing "mosaic" pattern and cement lines.

ularity of outline and distribution. A large number of small pieces of osseous tissue fitted together along prominent cement lines into a mosaic pattern, giving the classical appearance of Paget's disease. In many places the bony trabeculae were replaced by sheets of cells almost all of which had clear, homogeneous cytoplasm and pyknotic nuclei, although many of the nuclei were vesicular and eccentric. These cells had the characteristic appearance of myeloma cells. Within the tumor, numerous areas of hemorrhage and fibrosis were noted. Of the soft tissue organs, only the kidney and spleen showed histopathologic changes worthy of note. In the kidney, many of the tubules showed varying degrees of parenchymatous degeneration, but the most striking finding was the presence of proteinaceous material in the lumen. In addition, there were many foci of calcification, chiefly in the interstitial tissue, but also in a few areas involving the tubular epithelium. No myeloma cells were seen in the liver but the spleen showed increased cellularity of the pulp. This consisted of an active reticulum proliferation along with the presence of a moderate number of large cells with large vesicular nuclei whose chromatin was arranged in clumps. Occasional large cells with double nuclei were also seen. These had the histopathologic characteristic of myeloma cells. Calcification of the trabeculae was noted in a few places, but the significance of this observation is not too clear. Examination of the urine in the bladder at autopsy was positive for Bence-Jones protein.

DISCUSSION

The possibility of multiple myeloma in this patient was not entertained and the postmortem findings came as a surprise. Lichtenstein and Jaffe[3] believe that multiple myeloma is not uncommon and feel that many cases go unrecognized. They emphasize the significance of pain, particularly in the back and in the thorax. These complaints were present in our patient, but were difficult to evaluate because they could be so easily ascribed to the underlying Paget's disease. The presence of azotemia is a not infrequent indication of the presence of multiple myeloma and may occasionally dominate the clinical picture before multiple myeloma is even suspected.[3] Again, however, in our case, the presence of generalized arteriosclerosis and the suspicion of cardiovascular disease interfered with the proper evaluation of this finding. In contradistinction to multiple myeloma, osteogenic sarcoma is not uncommonly reported as a complication of Paget's disease. James Paget[4] himself called attention to this fact in his first publication on the subject and since then numerous reports have appeared in the literature. Reports on the percentage of cases undergoing malignant degeneration varies greatly with the geographic area and the type of material studied. In Europe the incidence is reported as lower than in the United States. In the American literature approximately 5 to 15 per cent of all cases of Paget's disease are thought to undergo malignant degeneration into osteogenic sarcoma. Other forms of malignant change may occur. Six cases of fibrosarcoma complicating Paget's disease were reviewed recently by Summey and Pressly.[8] Occasionally the changes in multiple myeloma may be confused with the changes found in Paget's disease. Geschickter and Copeland[2] found that roentgenograms were of particular diagnostic value when tumor formation was found in the skull. "The chief point of differentiation is the lack of increase of thickness of the skull im multi-

ple myeloma which is commonly found in Paget's disease. In Paget's disease the frontal cells are frequently diminished in size, whereas they are often enlarged in cases with multiple myeloma." When the disease entities are coexistent, as in this particular case, not only are the conditions difficult to differentiate, but apparently the changes due to Paget's disease are able to veil for a considerable period of time the characteristic changes due to the multiple myeloma.

CONCLUSION

A case of multiple myeloma complicating Paget's disease is discussed, in which the diagnosis was not suspected until revealed by postmortem. Although infrequently reported, the two conditions may coexist, but the Paget's disease is likely to obscure the myelomatous changes. Differentiation may be aided by roentgenological and laboratory procedures.

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CRANIOLACUNIA DIAGNOSED PRENATALLY*

REVIEW OF LITERATURE WITH A CASE REPORT

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THE prenatal diagnosis of craniolacunia is infrequently reported. The only article in the American literature appeared in 1934, when Maier[7] presented 2 cases. No further reference to the subject has been made, with the exception of Hartley and Burnett's outstanding contribution of 1943 in England.[2] Therefore, we feel that the present case report should be of interest

Craniolacunia was originally described in 1874 by Hoffman,[4] but it was not until 1907 that Markoe[8] reported a case in the American literature. No further mention of this condition was made until 1933, when Kerr[6] described the entity and reported 3 cases of his own. This was followed in 1934 by a paper by Doub and Danzer,[1] who reviewed the literature and reported 2 new cases. In the same year, Maier[7] presented 2 cases in which he made the diagnosis by prenatal roentgen examination of the maternal abdomen. He suggested that the diagnosis could be made by this method as early as the eighth month of gestation. No additional prenatal diagnoses of craniolacunia have been published in the American literature. However, Hartley and Burnett,[2] in the English literature (1943), reported 10 cases diagnosed prenatally. In addition, they state that the incidence is higher than generally thought, with an occurrence of 28 cases in 2,978 infants, an incidence of 0.94 per cent.

The association of other abnormalities in the infant with craniolacunia has been stressed by all authors. Vogt and Wyatt[10] in 1941 reported 54 cases of craniolacunia which were discovered by roentgenographing the skulls of all infants with meningocele. This represents a 43 per cent incidence of craniolacunia in cases of meningocele. However, 2 cases of this condition without accompanying meningocele were reported by the same authors. One was a hydrocephalic and the other was mentally deficient.

Craniolacunia is easily recognized by the roentgen appearance of large rounded areas of decreased density outlined by the web-like pattern of thicker bone. The sutures are usually not widened and no bulging is present in the anterior fontanel. The earlier reports considered increased intracranial pressure as the most likely etiological factor. However, pathological examination failed to substantiate this premise, since the convolutions of the brain did not correspond with the thinned areas of the skull. Further evidence brought to light by Hartley and Burnett[3] suggested the possibility of a nutritional factor playing a part in this condition. Considering this, they felt that there would be an increased incidence of craniolacunia following the war, especially in those countries where deficient diets were prevalent. Van Waalwijk *et al.*,[9] in a recent paper on this subject, suggest the same factor of a deficient prenatal diet in the mother as a possible cause. These authors report 5 cases of craniofenestria which they distinguish from craniolacunia, in that the latter only involves the inner table of the cranial bones. Most previous reports do not make this distinction. This condition had not been reported in The Netherlands before World War II and the infants were all conceived shortly after the war, which suggests that the maternal diet may have been a factor. Karshner and Reeves[5] in 1947 presented 7 cases of craniolacunia and, reviewing the literature as to etiology, concluded that the condition was a developmental defect.

Since the condition is readily recognized on the roentgenogram, its diagnosis should be simple. It is surprising, with the in-

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creased number of examinations of pregnant women by roentgen pelvimetry as well as survey films of the abdomen, that more cases diagnosed prenatally have not been reported. The frequent association of congenital abnormalities, particularly meningocele, makes a prenatal diagnosis a significant factor in the conduct of delivery. The case we present stresses this point.

CASE REPORT

A nineteen year old nulliparous white female was referred to the roentgenological department by the obstetrical division for cephalopelvimetry.

On the anteroposterior abdominal film, the fetal skull was seen to be somewhat irregular in contour and showed multiple rounded areas of radiolucency outlined by denser ridges of bone producing the web-like appearance so characteristic of craniolacunia. In addition, the lumbar spine presented a posterior angulation but no spina bifida or meningocele was identified. The remaining bony skeleton was normal and no polyhydramnios was present.

Unfortunately, a numerical dystocia at the inlet was present and, following a test of labor, it was decided to perform a caesarean section. The decision was made with full understanding that other abnormalities might be present and, if so, the fetal prognosis would be very bad. However, since there had been no definite accompanying abnormality demonstrable, the possibility of a craniolacunia alone was hoped for and with it a good chance for fetal survival.

At caesarean section, a living male child was delivered. There was a meningocele in the lumbar region measuring 10 by 7 cm. Bilateral talipes varus and imperforate anus were also present. Surgical consultants did not consider that correction of the imperforate anus was indicated, in view of the other findings. It was noted that meconium was passed from the penis.

The child died on the fourth day of life and an autopsy performed thirteen hours after death revealed the following: An imperforate anus was present, with the colon ending in a blind sac 3 cm. from the skin. A fistulous tract connected the colon to the prostatic urethra. There was maldescent of the cecum. The right kidney and ureter were entirely absent. The testes were not in the scrotum and could not be located elsewhere. The skull revealed multiple thinned areas with surrounding ridges of bone producing the lacunar skull. Both inner and outer tables were involved in the thinned areas and the latter were found to protrude slightly, externally. Complete perforation was not present. The underlying brain bulged slightly into these areas. Aside from this, the brain substance was not remarkable. The spinal cord revealed a meningomyelocele in the lumbar spine at L_3–L_4 levels. In the same area, a spina bifida deformity was present. An interesting feature in this case is the fact that the mother failed to adhere to the prescribed dietary regimen during her antepartum course and ate large quantities of sweets and other carbohydrate foods.

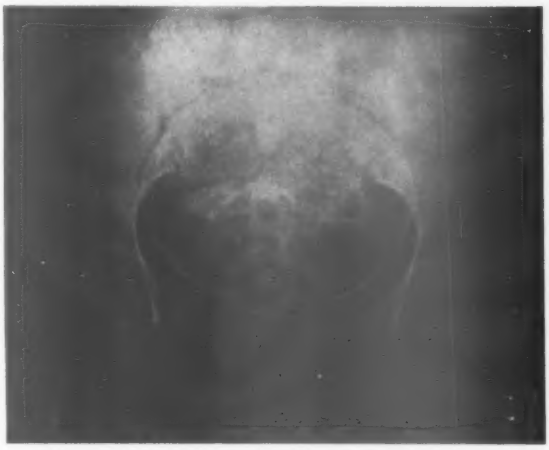

Fig. 1. Anteroposterior view of the maternal pelvis. The fetal skull is seen disclosing the characteristic findings of craniolacunia.

COMMENT

The pathological description would place this case in the craniofenestria type according to Van Waalwijk *et al.* Although complete penetration was not present, both inner and outer tables of the skull were involved in the thinned areas.

The multiple anomalies in this case would tend to support the theory of developmental defect as a possible etiological factor. Since a poor dietary regimen was apparently present in this case, the theory of malnutrition in the mother as a cause of the craniolacunia cannot be eliminated.

The unfortunate delivery of an abnormal child by caesarean section is regrettable.

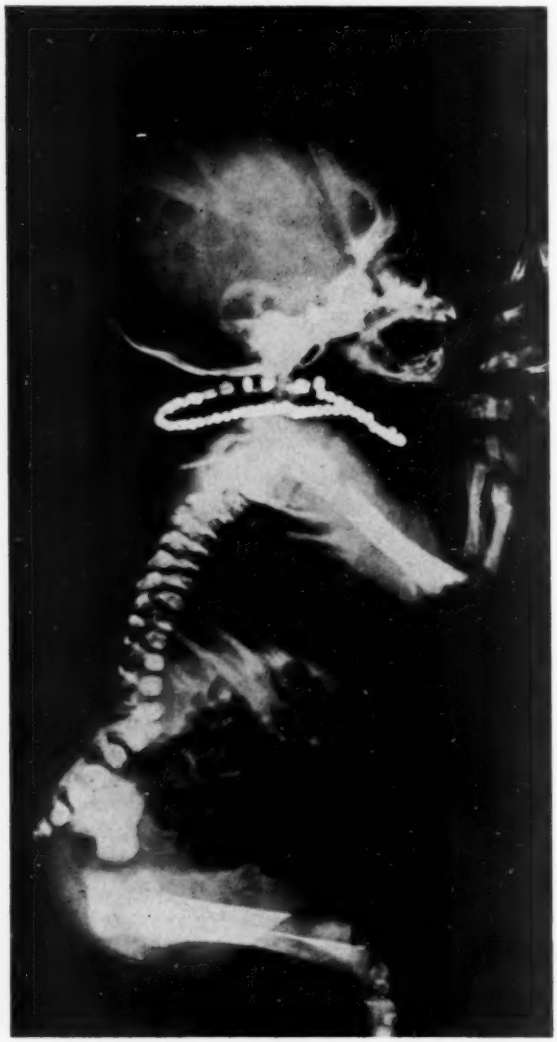

Fig. 2. Lateral view of the fetus, taken shortly after birth. The craniolacunia is clearly demonstrated. The meningocele can be seen lying near the area of angulation in the lumbar spine. This was the region of spina bifida.

The demonstration of craniolacunia indicates an abnormal fetus, but most physicians probably would prefer additional evidence of abnormality before altering their plan of treatment. In this case, clear demonstration of spina bifida was not possible. However, careful search for fetal abnormality is indicated in cases of craniolacunia diagnosed prenatally. This point is stressed by Hartley and Burnett who state that craniolacunia itself is of little danger to the life of the child, although its occurrence alone is rare. The demonstration of associated anomalies is important as it may dictate a change in the conduct of labor.

SUMMARY

1. A brief review of the literature on craniolacunia is given.

2. A case of craniolacunia diagnosed prenatally is presented.

3. Multiple anomalies in this case support the theory of developmental abnormality as a possible etiological factor.

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ESTIMATION OF THE WEIGHT OF THE HYPERPLASTIC PROSTATE FROM THE CYSTOURETHROGRAM*

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MANY urologists today use, as one of the deciding factors for the method of prostatectomy to be employed on the hyperplastic gland, its estimated weight. The dividing line when considering weight usually depends on the urologist and his proficiency with the resectoscope.

From the anteroposterior view of the cystourethrogram, a method has been devised for estimating the weight of the hyperplastic tissue. The method depends on a formula and the correct manner in taking the anteroposterior view. A description of the procedure for making cystourethrograms and their interpretation may be found in an article by myself and Randall.[1] Two essential points will be emphasized. First, the roentgen tube is adjusted to 36 inches from the cassette, and second, the tube is centered over the pubis.

By measuring in centimeters on the cystourethrogram, the horizontal and vertical diameters of the prostatic mass, and from these, finding the average diameter, the estimated weight of the hyperplastic gland can be readily interpolated from a conversion chart.

In order to understand the measurements, one must first visualize the hyperplastic gland as a sphere, oval or round. This can easily be noted by inspecting a hyperplastic prostate recently enucleated *in toto*.

Since hyperplasia takes place proximal to the verumontanum, this imprint on the cystourethrogram is taken as the distal point of the vertical measurement. The other point is the most superior extent of the prostatic mass as seen on the cystourethrogram. This gives the vertical diameter. At times the imprint of the verumontanum cannot be discerned accurately, but the external sphincter, which is usually more easily made out, can be used as the distal extent, subtracting from the vertical diameter 1.5 centimeters, which is the average distance from the upper end of the external sphincter to the upper end of the verumontanum.

Some procedures for estimating the weight of the prostate have been based on the prostatic urethral lengthening, but I believe that inspection of the oblique view of a trilobar hyperplasia with anterior tilting will reveal the error in these procedures, as one is not measuring the diameter of the prostatic mass, but a urethra bent to various degrees through the mass.

The horizontal diameter is found by measuring the distance between each lat-

TABLE I

PROSTATIC DIAMETER TO WEIGHT CONVERSION CHART FOR CYSTOURETHROGRAMS

Diameter cm.	Weight gm.	Diameter cm.	Weight gm.	Diameter cm.	Weight gm.
3.2	8	5.2	34	7.2	93
3.4	10	5.4	38	7.4	101
3.6	11.5	5.6	44	7.6	110
3.8	14	5.8	49	7.8	119
4.0	16	6.0	54	8.0	128
4.2	18.5	6.2	59.5	8.2	138
4.4	21	6.4	65.5	8.4	148
4.6	24	6.6	72	8.6	159
4.8	27	6.8	78.5	8.8	170
5.0	30.5	7.0	86	9.0	182

* Read before the Detroit Branch of the American Urological Association, May 4, 1949.

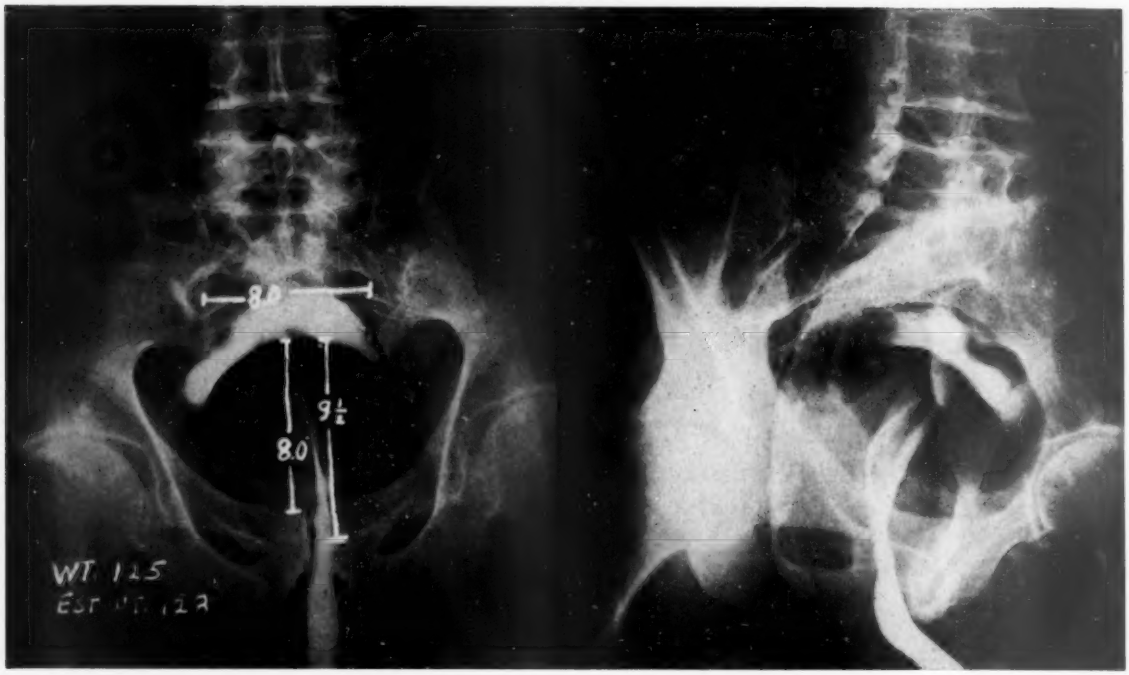

Fig. 1. An anteroposterior and oblique cystourethrogram of a hyperplastic prostate demonstrating how the measurements may be made on the anteroposterior film for use in the conversion table. In this case both the vertical and horizontal diameters are 8 cm. The vertical diameter to the proximal border of the external sphincter is 9.5 cm. from which 1.5 cm. is subtracted for the true diameter. The average diameter is 8 cm., and from the conversion table this gives an estimated weight of 128 gm. The actual weight was 125 gm.

eral margin of the prostatic mass at its widest part.

The average diameter of the horizontal and vertical measurements is calculated for use in the conversion table (Table 1).

The conversion table is merely made up for convenience. The weights were originally arrived at by completing the formula, radius cubed times two equals weight in grams of the prostatic adenoma ($R^3 \times 2 = W$). The formula was discovered by accident and why it succeeds cannot be reasoned.

Over one hundred consecutive cases reveal that in prostatic adenomas weighing

Fig. 2. An example of a hyperplastic prostate with a horizontal diameter of 6 cm., a vertical diameter of 5.5 cm. (vertical diameter to external sphincter is 7 cm. from which the constant 1.5 cm. is subtracted to give 5.5 cm.), and an average diameter of 5.75 cm. From the conversion table this gives a hyperplastic prostate of 49 gm. The actual weight was 52 gm.

25 grams or less, the estimated weight has been within 4 grams of the actual enucleated weight; for those between 25 and 50 grams, the estimated weight has been within 8 grams; and for those over 50 grams, it has been within 10 grams.

CONCLUSION

For practical purposes, the weight of a benign hyperplastic prostate can be readily and accurately determined from the antero-posterior projection of the cystourethrogram.

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ANDROGEN THERAPY IN THE CONTROL OF PULMONARY METASTASIS FROM ADENO-CARCINOMA OF THE CORPUS UTERI

REPORT OF A CASE BENEFITED BY ANDROGEN THERAPY*

By JOHN H. FREED, M.D., EUGENE P. PENDERGRASS, M.D., *and* JOHN W. CARNWATH, M.D.

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DURING the past few years, increasing attention is being given to the possible role of abnormal hormonal stimuli in tumor genesis, particularly in those tumors arising in certain tissues of the reproductive organs whose normal growth and function are known to be dependent on the effects of the various gonadal hormones. While these gonadal hormones in themselves are generally not regarded as carcinogenic, it is believed that they may provide the substrate upon which some other extrinsic or intrinsic exciting agent may act to produce the tumor.

Evidence has now been accumulated through experimental and clinical studies which seem to indicate that the gonadal hormones have some direct or indirect influence on the development and growth of carcinoma of the breast,[13] and although their mechanism of action is poorly understood, the value of artificial sterilization[18,21] and supplementary androgen therapy[8] to inhibit the futher growth and spread of the disease has been fairly well established.

The studies of Huggins and his coworkers[10,11] on prostatic cancer have shown that the androgenic hormones have a definite stimulating effect on the growth of this tumor and that castration and supplementary estrogen therapy is of real value in the treatment.

What influence the estrogenic hormones may have on the origin and growth of endometrial carcinoma still remains open to question. A theory of hyperestrinism was proposed many years ago by Witherspoon[25] as a cuase of fibromyoma of the uterus, but this is disputed by other authors.[2] The case for a hormonal factor in the etiology of fibroids rests chiefly on the atrophy which occurs following removal or destruction of ovarian function. Evidence is accumulating which seems to indicate that endometrial hyperplasia results from ovarian dysfunction.[7,9,14,17,22,23,26] Though endometrial hyperplasia is regarded as a possible precancerous lesion by some authors who have reported the frequent development of a carcinoma in a hyperplastic endometrium,[9,14,17,22] others insist that the association is no more than accidental.[2,15] While this controversy continues, another group of cases is being reported which seem to constitute the most important evidence for an estogenic factor in endometrial carcinoma. These are the cases which have been observed with an associated granulosa cell or theca cell tumor of the ovary and adenocarcinoma of the endometrium. Patients with a granulosa cell tumor of the ovary and associated endometrial carcinoma have been reported by Stohr,[19] Ingraham and his associates,[12] and by others.[24] Case records of carcinoma of the endometrium in association with theca cell tumors are reported by Porter and Bramhall,[16] Dockerty,[4] and Taylor.[23] Estrogen therapy, particularly stilbestrol, has been suggested as the cause of several endometrial carcinomas.[6,20]

In view of these studies which seem to suggest a possible estrogenic factor in endometrial carcinoma, and the palliative results achieved through the use of androgen therapy in breast cancer, a clinical therapeutic trial of androgen therapy seemed warranted in certain selected cases

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of endometrial cancer. Since it seemed unwise to withhold the accepted forms of treatment, surgery and irradiation, in order to evaluate the effects of androgen therapy, such hormone therapy must be reserved for advanced hopeless cases. Abel[1] in 1944 made such a study on 5 advanced, hopeless cases after other orthodox methods of treatment had failed. In a preliminary report on these patients he noted some subjective improvement, but found nothing to indicate that there was any regression of the malignant process in any of these patients following androgen therapy.

Another method of evaluating the effects of androgen therapy in endometrial carcinoma, without denying the patient any of the accepted modes of treatment, would be to use the androgens as the sole method of treatment of any widespread metastatic disease, with surgery or irradiation utilized to treat the primary growth or advanced disease in the pelvis. We decided to make such a study when a patient was referred to us with advanced endometrial carcinoma in the pelvis and metastasis to the right tibia and lung fields. A therapeutic trial of androgen therapy in this patient caused such a remarkable regression of the pulmonary metastatic lesions that it seemed worth while to report the case in detail.

CASE REPORT

A. J., (No. 19093), a white woman, aged fifty-five, was referred to the Jeanes Hospital tumor clinic on January 25, 1949, following a biopsy of a nodular mass on the posterior vaginal wall, taken by her family physician, and reported as metastatic adenocarcinoma. She gave a history of occasional vaginal spotting since June, 1948; was a para II, with a normal menstrual history and passed through her menopause at the age of fifty-three.

Physical Examination. This disclosed a well developed, well nourished, middle aged, white woman. A small soft tissue mass was noted on the anterior surface of the right lower leg which was firm, hard, and slightly tender. Pelvic examination revealed four small, firm, hard nodules of 1 to 2 cm. diameter along the upper anterior and posterior vaginal walls with two large nodular growths, each about 4 cm. in diameter, located near the external urethral meatus. The parametria were free, the cervix clean, and the uterus freely movable but enlarged to about the size of a two months pregnancy.

Laboratory Studies. These were essentially normal, except for a 4 plus Wassermann reaction.

Roentgenographic Studies. Roentgenograms of the chest revealed multiple, small, nodular, metastatic parenchymal lesions in the right lower lung field, with three or four scattered lesions in the remainder of the lung fields (Fig. 1*A*). A single osteolytic lesion was noted in the lower half of the right tibia (Fig. 2*A*). A urographic study showed a normal bilaterally functioning urinary tract.

Operations. Dilatation and curettage of the uterus revealed a large amount of friable tissue appearing grossly malignant. An aspiration biopsy of the soft tumor mass on the right tibia was performed.

Pathological Report. Adenocarcinoma, Grade 2 of the corpus uteri. Metastatic adenocarcinoma of right tibia.

Treatment Plan. Combined intracavitary radium and external roentgen therapy to the pelvis with possible supplementary androgen therapy for chest metastasis. External roentgen therapy to lesion, right tibia.

Intracavitary Radium Therapy. Six radium tubes (each 2.17 cm. external length, 1.5 cm. active length, 1 mm. platinum filtration and containing 13.33 mg. of radium) were placed in tandem in a rubber catheter. This flexible rubber catheter was inserted and manipulated so that two radium tubes lay along each lateral wall and two along the superior wall of the uterus. The treatment time was fifty hours for 4,000 milligram hours. A second similar application was given two weeks later for a total of 8,000 mg. hr. The minimum tumor dose along the external wall of the uterus was estimated as 3,000 gamma roentgens.

Roentgen Therapy. Factors 200 kv., 20 ma., 0.5 mm. Cu plus 1 mm. Al, half-value layer 1.0 Cu, 50 cm. skin target distance.

A 10 by 15 cm. anterior and posterior field was directed to each side of the pelvis and a total mid-pelvic dose of 2,500 roentgens was given in seven weeks. This was supplemented by intravaginal cone therapy directed to the two large 4 cm. vaginal lesions located about the

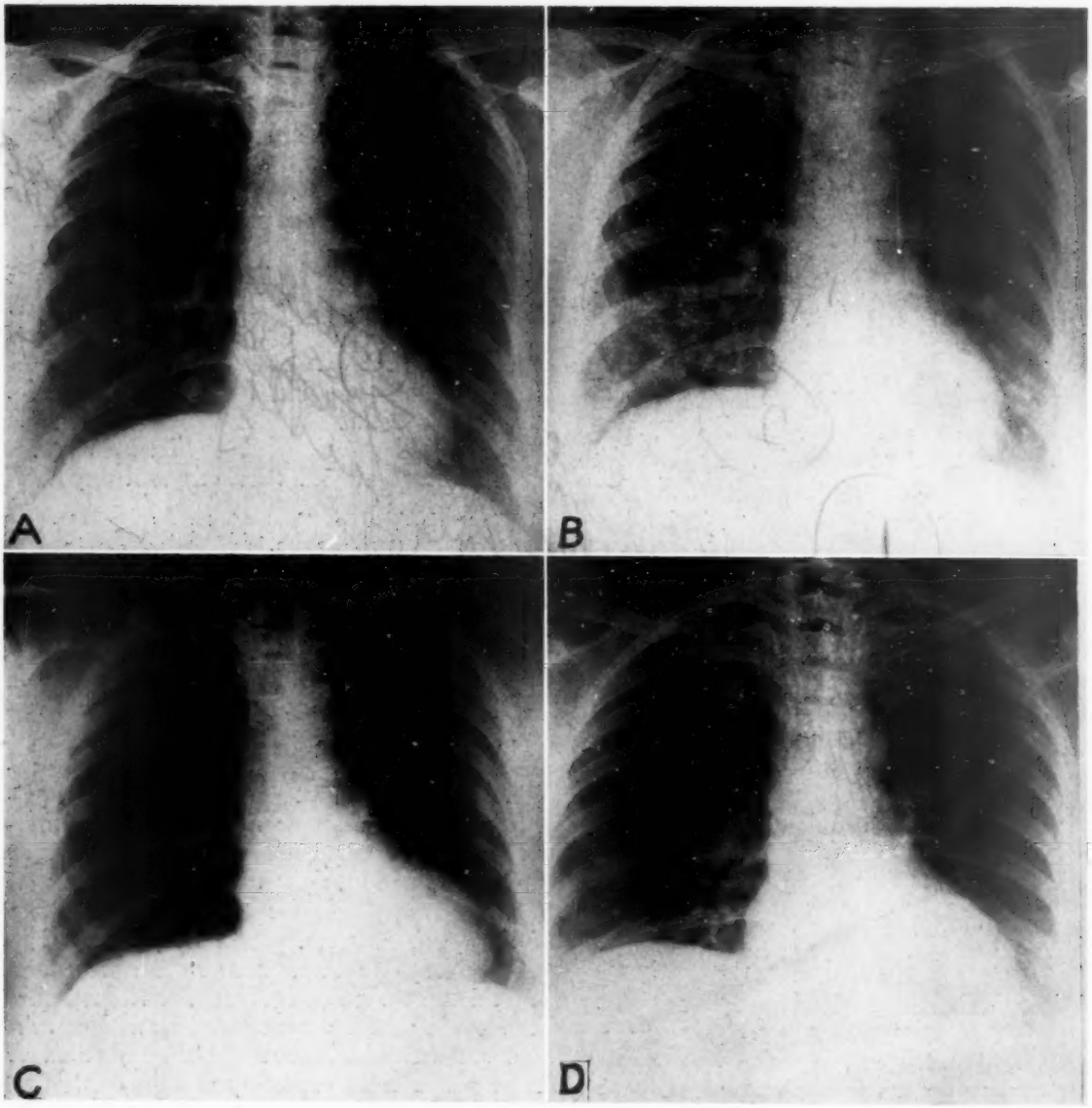

Fig. 1. Pulmonary metastasis from an advanced adenocarcinoma of the corpus uteri. (*A*) January 25, 1949. Appearance of chest when patient first seen. (*B*) June 29, 1949. Marked increase in parenchymal metastasis. (*C*) September 19, 1949. Complete regression of parenchymal metastasis following testosterone propionate injections. (*D*) March 27, 1950. Beginning recurrence of parenchymal metastasis in the right lower lung field.

external urethral meatus for an additional tumor dose of 3,000 r to these lesions.

A small field was used over the right tibial lesion and a tumor dose of 1,500 r delivered in two weeks.

Note: It was decided to withhold *androgen therapy* until the appearance of chest symptoms.

Result. A pelvic examination on April 19, 1949, showed no evidence of residual disease in the pelvis. The uterus remained slightly enlarged.

Follow-up. The patient remained asymptomatic, except for occasional slight pain in the tibia, until June 29, 1949. Roentgenograms of the right tibia now revealed a new smaller osteolytic lesion just below the large osteolytic lesion (Fig. 2*B*). Some calcification was seen about the treated lesion. The patient was complaining of a dry hacking cough and another

Fig. 2. Metastasis to right tibia from an advanced adenocarcinoma of the corpus uteri. (*A*) January 25, 1949. Single osteolytic lesion in right tibia. (*B*) June 29, 1949. New smaller osteolytic lesion just below the large osteolytic lesion in right tibia. Some calcification is noted about the large osteolytic lesion following roentgen therapy. (*C*) July 2, 1949. Pathological fracture of right tibia. (*D*) March 27, 1950. No evidence of healing of the pathological fracture of right tibia after nine months of immobilization in a cast.

chest roentgenogram showed a rather marked increase in the number of metastatic parenchymal nodules (Fig. 1*B*).

Additional Treatment. The patient was started on testosterone propionate (oreton) 100 mg. I.M., three times weekly, and additional roentgen therapy was given to the right tibia, to a tumor dose of 4,000 r in three weeks. The pain

in the right tibia was completely relieved, and the patient was discharged to the care of her family physician with instructions to guard the right leg in walking and to continue the testosterone injections. Three days later she suffered a fracture of her right tibia while getting off a bus and was readmitted to the Jeanes Hospital. Roentgenograms revealed a pathological fracture of the right tibia (Fig. 2*C*). This was reduced and a cast applied. She was again discharged home to the care of her family physician and instructed to continue the testosterone injections.

Follow-up Continued. The patient was asymptomatic on her next visit to the Jeanes Hospital Follow-up Clinic on September 19, 1949. Roentgenograms of the chest showed a complete regression of the previous metastatic parenchymal lesions (Fig. 1*C*). A roentgenogram of the tibia showed no change in the appearance of the osteolytic bone lesions. She had received a total of 3,300 mg. of oreton up to this date. There was noticeable deepening of her voice and considerable facial hirsutism, but these masculinizing effects were not disturbing to her. The leg cast was reapplied; the oreton was discontinued, and the patient discharged home.

During subsequent follow-up visits at four to to six week intervals, she remained asymptomatic without evidence of recurrent chest metastasis.

A roentgenogram of the chest (Fig. 1*D*) made during her last follow-up visit on March 27, 1950, revealed two or three small nodular lesions in the right lower lung field resembling early recurrent metastasis. Roentgenograms of the tibia still showed no evidence of beginning union (Fig. 2*D*). She continues to remain asymptomatic and an attempt is now being made to fit her with a walking caliper to allow her to become more active, with the hope that this might stimulate healing of the fracture.

DISCUSSION

Two interesting features about this case seem worthy of further comment. These are the prompt disappearance of chest metastasis following a course of testosterone propionate injections and the failure of healing of the pathological fracture in the right tibia with conservative management.

The fact that androgen therapy was effective in causing a complete regression of the chest metastasis with no evidence of a recurrence for six months seems to provide further evidence of a hormonal factor in the etiology and growth of endometrial carcinoma. If this hormonal factor in endometrial carcinoma is due to a continued abnormal estrogen stimulation, then the beneficial effects of androgen therapy might be attributed to an interference of the androgens with estrogen activity. According to Burrow,[3] the androgens may interfere with estrogen activity in several ways: (1) they may directly inhibit the organ's response to estrogen; (2) they may check the supply of estrogen from the ovary by preventing the output of gonadotropin from the pituitary; or (3) they may perhaps oppose the action of gonadotropin on the ovary.

If estrogen secretion by the ovary alone represented the apparent hormonal stimulus to the growth of the pulmonary metastasis in this patient, one might have expected a regression of the pulmonary metastasis following the rather large amount of radiation delivered to the pelvic growths and ovaries. Instead there was a continued progression of the pulmonary metastasis.

It would seem that any continued estrogen stimulation following the radiation treatment must have resulted from an extragonadal source of estrogen, such as the adrenal cortex. Another possible hormonal stimulus could have been mediated through an increase in the output and potency of gonadotropic hormone by the pituitary which is known to occur at the menopause[5] or after roentgen sterilization or surgical castration.[27] It is possible that the increased supply of gonadotropin could act as a primary stimulus to the tumor growth, or secondarily by stimulating an increased secretion of estrogen from the adrenal cortex.

Though the mechanism of action of the androgens remains obscure, the favorable effects achieved in this patient following androgen administration lend further sup-

port to the belief that some hormonal imbalance between the anterior pituitary, adrenal cortex, and ovary may play an important part in the genesis and growth of endometrial carcinoma.

The failure of healing of the pathological fracture in the right tibia after nine months of immobilization was also an unusual finding in this patient. In our own experience with the management of pathological fractures, secondary to metastatic bone lesions from the breast and other tumors, healing has usually resulted after a reasonable period of immobilization, even though the lesion had been previously treated by roentgen therapy.

SUMMARY

1. The evidence for an estrogenic factor in the genesis and growth of endometrial carcinoma is briefly reviewed.

2. A case of advanced carcinoma of the uterus with metastasis to the vagina, right tibia, and lung fields is presented with an outline of the radiation treatment and supplementary androgen therapy given and the results of the treatment.

3. Following radiation therapy to the ovaries and tumor growth in the uterus and vagina, there was a fairly rapid progression of the untreated pulmonary metastasis.

4. A complete regression of the pulmonary metastasis, without evidence of recurrence for six months, following androgen therapy, suggests that a hormonal stimulus to these metastatic growths may have been present which was inhibited by the androgen. The possible mechanism of action of the administered androgen is discussed.

5. The favorable effects achieved in this patient following androgen therapy seem to suggest that the androgens may prove to be a useful adjuvant to the already accepted modes of therapy—surgery and irradiation—in the treatment of advanced endometrial carcinoma.

6. The failure of healing of a pathological fracture in the right tibia of this patient after nine months of immobilization is an unusual occurrence in our experience with the management of pathological fractures from other types of metastatic tumors where healing has usually resulted after a reasonable period of immobilization.*

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* We are grateful to the Schering Corporation, Bloomfield, New Jersey, for the generous supply of oreton (testosterone propionate) used in the treatment of this patient.

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INTERNATIONAL RECOMMENDATIONS ON RADIOLOGICAL PROTECTION

REVISED BY THE INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION AT THE SIXTH INTERNATIONAL CONGRESS OF RADIOLOGY (LONDON, JULY, 1950)

Report Prepared by Members of the International Commission on Radiological Protection as Follows:

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INTRODUCTION

DEVELOPMENTS in nuclear physics and their practical applications since the Fifth International Congress of Radiology have greatly increased the number and scope of potential hazards. At the same time, biological research has led to an extension of our knowledge of the dangers associated with ionizing radiations. This increase of biological knowledge has not only brought a realization of the importance of certain effects, particularly carcinogenic and genetic effects, but has also provided more information as to the permissible levels of radiation. The International Commission on Radiological Protection has therefore adopted new radiation safety standards with more rigid criteria. Such standards must, in view of the still limited experience of the effects of radiation, be kept continually under review.

It appears that the effects to be considered are:

(1) Superficial injuries.
(2) General effects on the body, particularly the blood and blood-forming organs, e.g., production of anemia and leukemias.
(3) The induction of malignant tumors.
(4) Other deleterious effects, including cataract, obesity, impaired fertility, and reduction of life span.
(5) Genetic effects.

While it is still fundamental to express whole body exposure in terms of a single number, it is not practicable, in general, in view of the complexity of circumstances now arising, to express the maximum permissible hazards in terms of a single parameter. It is, for example, highly desirable to derive values of maximum permissible concentrations of radioactive materials, in the air or in drinking water, taking into account the metabolism of the materials concerned, and assuming standard anatomical, physiological and chemical data. Furthermore, the previously accepted value of 1 roentgen per week for maximum permissible exposure to external radiation itself needs revision in the light of the nature of the radiations to which workers are now exposed. There is the added difficulty that the roentgen is not an acceptable unit of dose for all ionizing radiations. Accordingly, the following recommendations are based on considerations of the equivalent energy absorbed in tissue, coupled with the appropriate relative biological efficiency.

While the values proposed for maximum permissible exposures are such as to involve a risk which is small compared to the other hazards of life, nevertheless, in view of the unsatisfactory nature of much of the evidence on which our judgments must be based, coupled with the knowledge that certain radiation effects are irreversible and cumulative, it is strongly recommended that every effort be made to reduce exposures to all types of ionizing radiations to the lowest possible level.

EXPOSURE TO EXTERNAL RADIATION

1. *Exposure of Individuals to Roentgen, Gamma, and Beta Radiation.*

(a) *Whole body exposure.* A careful consideration of the deleterious biological effects enumerated in the Introduction, in the light of observations on man and of the experimental data on animals, has led to the conclusion that, insofar as the well-being of the individual is concerned, the most dangerous effects of external radiation are probably those on the blood-forming organs. Although the dose to these organs is regarded as a fundamental quantity, for practical reasons the maximum permissible exposure is best stated in terms of the surface dose per week. The figure of 1 r per week previously adopted by the International X-ray and Radium Protection Commission seems very close to the probable threshold for adverse effects, particularly for radiations of high energy which are more frequently encountered than formerly. A reduction of surface dose is therefore called for. For these reasons and for those previously outlined in the Introduction, it is recommended that:

(i) *In circumstances under which the whole body may be exposed over an indefinite period to roentgen or gamma radiation of quantum energy less than 3 mev., the maximum permissible dose received by the surface of the body shall be 0.5 roentgen in any one week. This dose corresponds to 0.3 r per week measured in free air.*

(ii) *In the case of high energy beta rays, the maximum permissible exposure of the surface of the body in any one week shall be the energy flux of beta radiation such that the absorption per gram of superficial tissues is equivalent to the energy absorption from 1.5 roentgens of hard gamma rays.*

For purposes of calculation, the superficial tissues concerned shall be assumed to be the basal layer of the epidermis, defined conventionally as lying at a depth corresponding to 7 mg./cm².

(b) *Critical tissues.* The recommendations relating to exposure to external radiation are primarily framed in relation to exposure of the whole body. Nevertheless, a greater exposure should not be permitted for irradiation confined to a particular organ or tissue, except in the case of the hands and forearms. Measurements may be made either in air or at the surface of the body with backscatter, and it is estimated that the surface dose of 0.5 r of penetrating electromagnetic radiation would correspond roughly to 0.3 r at the critical tissue, namely, the blood-forming organs, conventionally assumed to lie at a depth of 5 cm. below the surface. This figure of 0.3 r is the fundamental figure which is though appropriate for the irradiation of any critical tissue, with the one obvious exception of the skin.

(c) *Partial exposure.* It is recommended that:

In the case of exposure of the hands and forearms to roentgen, gamma and beta radiation, the maximum permissible dose shall be 1.5 r (or its energy equivalent) in any one week, at the basal layer of the epidermis, defined conventionally as lying at a depth corresponding to 7 mg./cm².

2. *Whole Body Exposure of Individuals to Neutrons.*

The International Commission on Radiological Protection considers that the maximum permissible energy absorption per gram of tissues exposed to fast neutrons should not be greater than one-tenth of that permitted for high energy quantum radiation. The Commission is presently in the process of collecting data as a basis for future numerical recommendations.

EXPOSURE TO INTERNAL RADIATION

3. While the Commission does not, at the moment, consider that there is sufficient information to make firm recommendations concerning maximum permissible exposures to internal radiation from radioactive isotopes, it brings to the notice of users of radioactive isotopes values which are commonly used, at the present time, in the United States of America, Canada and Great Britain. These values will appear in a

supplementary document to be prepared and circulated by the Commission.

The Commission will continually review these values as new information becomes available, and will, if necessary, circulate amended values.

I. WORKING CONDITIONS

4. The following conditions are recommended for radiation workers:

(a) The amount of radiation received by operators should be systematically checked to insure that the maximum permissible dose is not exceeded. For this purpose, photographic films or small ionization condensers should be carried on the person.

(b) In addition, radiation workers should be systematically submitted, both on entry and subsequently, to expert blood examinations every three months, and to medical and general examinations once a year, special attention being paid to the hands. These examinations will determine the acceptance, refusal, limitation or termination of occupation involving radiation exposure.

II. GENERAL ROENTGEN-RAY AND RADIUM RECOMMENDATIONS

5. All rooms should be provided with adequate ventilation. In certain climates it may be necessary to have recourse to air conditioning. For rooms of normal dimensions, say 3,000 cubic feet (90 m.^{3}), in which corona-free apparatus is installed, the ventilating system should be capable of renewing the air of the room not less than six times per hour, while up to ten times may be required when the apparatus is not corona-free. Large rooms require proportionately fewer changes of air per hour than small ones. Air inlets and outlets should be arranged to afford cross-wise ventilation of the room.

6. All rooms should preferably be decorated in light colors.

7. A working temperature of about 18°–22° C. (65°–72° F.) is desirable in roentgen-ray rooms.

8. Roentgen-ray rooms should be large enough to permit a convenient lay-out of the equipment. A minimum floor area of 250 sq. ft. (25 m.^{2}) is recommended for roentgen-ray rooms, and 100 sq. ft. (10 m.^{2}) for darkrooms. Ceilings should be not less than 11 ft. (3.5 meters) high.

9. High-tension generators having exposed high-tension systems should preferably be placed in a separate room from the roentgen tube.

III. ROENTGEN-RAY PROTECTIVE RECOMMENDATIONS

10. A roentgen-ray operator should on no account expose himself to a direct beam of roentgen rays.

11. An operator should place himself as remote as practicable from the roentgen tube. It should be borne in mind that valve tubes are capable of producing roentgen rays.

12. The roentgen tube should be self-protected, or otherwise surrounded as completely as possible with protective material of adequate lead equivalent.

13. Barriers of protective material against primary and secondary radiation should be erected and should be of sufficient thickness to reduce the radiation level at any point of occupancy to the permissible levels stated above.

(A) *Diagnostic Work.*

14. In the case of diagnostic work with other than completely protected tubes, the operator should be afforded additional protection from stray radiation by a screen of a minimum lead equivalent of 1 millimeter.

15. Screening examinations should be conducted as rapidly as possible with minimum intensities and apertures, particularly when fractures are reduced under roentgen rays. Palpation with the hand should be reduced to the minimum.

16. The lead glass of fluorescent screens should be of sufficient thickness to reduce the radiation to the permissible level.

17. In the case of screening stands, the fluorescent screen should, if necessary, be provided with a protective "surround," so

that adequate protection against direct radiation is afforded for all positions of the screen and diaphragm.

18. Screening stands and couches should provide adequate arrangements for protecting the operator against scattered radiation from the patient.

19. Protective gloves, which should be suitably lined with fabric or other material, should have a protective value not less than 0.33 millimeter of lead throughout both back and front (including fingers and wrist). Protective aprons should have a minimum lead value of 0.5 millimeter.

(B) *Treatment.*

20. In the case of roentgen treatment, the operator is best stationed completely outside the roentgen-ray room behind a protective wall, the lead equivalent of which will depend on the circumstances. In the case of a single roentgen tube excited by voltages up to 200 kv., the protective wall should have a minimum lead equivalent of 2 millimeters. This figure should be increased in the case of higher exciting voltages or of heavy tube-currents so as to reduce the radiation at any point of occupancy to the agreed permissible level. In such event, the remaining walls, floor and ceiling may also be required to provide supplementary protection for adjacent occupants to an extent depending on the circumstances. Full protection should be provided in all those directions in which the direct beam can operate. Inspection windows in screens and walls should have protective lead values equivalent to that of the surrounding screen or wall.

21. In those cases in which a roentgen tube is continuously excited, and treatment periods are regulated by means of a shutter, some form of remote control should be provided for the shutter, to insure that the operator is not exposed to direct radiation while manipulating the shutter or filter.

22. Efficient safeguards should be adopted to avoid the omission of a metal filter in roentgen treatment, for example, by an interlocking device or by continuously measuring the emergent radiation. Protective screens and applicators (cones) used in treatment to define the ports of entry of roentgen-ray beams should be sufficiently thick to reduce the dosage rate outside the direct field of irradiation to less than 2 per cent that of the direct beam.

IV. ELECTRICAL PRECAUTIONS IN ROENTGEN-RAY ROOMS

23. The floor-covering of the roentgen-ray rooms should be of insulating material such as wood, rubber or linoleum.

24. Where permanent overhead conductors are employed, they should be not less than 9 ft. (3 meters) from the floor. They should consist of stout metal tubing or other coronaless type of conductor. The associated connecting leads should be of coronaless wire kept taut by suitable rheophores.

25. Wherever possible, earthed guards or earthed sheaths should be provided to shield the more adjacent parts of the high-tension system. Unshielded leads to the roentgen tube should be in positions as remote as possible from the operator and the patient. The use of "shock-proof" roentgen-ray equipment, in which the high-tension circuit is completely enclosed in earthed conductors, is recommended. In all cases, however, indiscriminate handling of roentgen tubes during operation should be forbidden. Unless there are reasons to the contrary, metal parts of the apparatus and room should be efficiently earthed.

26. Main and supply switches should be very accessible and distinctly indicated. They should not be in the proximity of the high-tension system, nor should it be possible for them to close accidentally. The use of quick-acting, double-pole circuit breakers is recommended. Over-powered fuses should not be used. If more than one apparatus is operated from a common generator, suitable high-tension, multi-way switches should be provided. In the case of some of the constant potential generators,

a residual charge is held by the condensers after shutting down, and a suitable discharging device should therefore be fitted. Illuminated warning devices which operate when the equipment is "alive" serve a useful purpose. The staff should be trained in the use of first-aid instructions dealing with electrical shock. If foot switches are used, they should be connected in series with an ordinary switch, and should be so designed that they cannot be locked to keep the circuit "alive," and are not capable of being closed accidentally.

27. Some suitable form of kilovoltmeter should be provided to afford a measure of the voltage operating the roentgen tube.

28. Low flash-point anesthetics should never be used in conjunction with roentgen rays.

V. FILM STORAGE PRECAUTIONS

29. The use of non-inflammable roentgen films is strongly recommended. In the case of inflammable films, suitable precautions should be taken as regards their use and storage. Large stocks should be kept in isolated stores, preferably in a separate building or on the roof.

VI. RADIUM PROTECTIVE RECOMMENDATIONS

(A) *Radium Salts.*

30. Protection for radium workers is required from the effects of:

(a) Beta rays upon the hands.
(b) Gamma rays upon the internal organs, vascular and reproductive systems.

31. In order to protect the hands from beta rays, reliance should be placed, in the first place, on distance. The radium should be manipulated with long-handled forceps, and should be carried from place to place in long-handled boxes, lined on all sides with at least 1 centimeter of lead. All manipulations should be carried out as rapidly as possible.

32. Radium, when not in use, should be stored in a safe as distant as possible from the personnel. It is recommended that the safe should be provided with a number of separate drawers individually protected. In the table below will be found the thicknesses of lead which will reduce the radiation to permissible levels at various distances from the source.

33. A separate room should be provided for the "make-up" of screened tubes and applicators, and this room should only be occupied during such work.

34. In order to protect the body from the penetrating gamma rays during handling of radium, a screen of not less than 2.5 centimeters of lead should be used, and proximity to the radium should only occur during actual work, and for as short a time as possible.

35. The measurement room should be a separate room, and it should preferably contain the radium only during its actual measurement.

36. Nurses and attendants should not remain in the same room as patients undergoing radium treatment with quantities exceeding 0.5 gram.

37. All unskilled work, or work which can be learned in a short period of time, should preferably be carried out by temporary workers, who should be engaged on such work for periods not exceeding six months. This applies especially to nurses and those engaged in "making-up" applicators.

38. Radium containers should be tested periodically for leakage of radon. Prejudicial quantities of radon may otherwise accumulate in radium safes, etc., containing a number of leaky containers.

39. Information regarding the quantity of radium and type of transport container, which will be accepted for transmission by land, sea or air, should be obtained from the appropriate Transport Authorities in the individual countries.

(B) *Radon.*

40. In the manipulation of radon, protection against beta and gamma rays is

required, and automatic or remote controls are desirable.

41. The handling of radon should be carried out, as far as possible, during its relatively inactive state.

42. Precautions should be taken against excessive gas pressures in radon plants. The escape of radon should be very carefully guarded against, and the room in which it is prepared should be provided with an exhaust fan controlled from outside the room.

43. Where radon is likely to come in direct contact with the fingers, thin rubber gloves should be worn to avoid contamination of the hands with active deposit. Otherwise the protective measures recommended for radium salts should be carried out.

44. The pumping room should preferably be contained in a separate building. The room should be provided with a connecting tube from the special room in which the radium is stored in solution. The radium in solution should be heavily screened to protect people working in adjacent rooms. This is preferably done by placing the radium solution in a lead-lined box, the thickness of lead recommended being according to the table below.

(C) *Radium Beam Therapy.*

45. The risks to the operator attendant on the use of large quantities of radium in radium beam therapy may be largely obviated if some system of remote control is adopted by which the radium is only introduced into the "bomb" after the latter has been adjusted in position on the patient. If such arrangements are not available the importance of expeditious handling is stressed.

46. Rooms used for radium beam therapy should provide adequate protection for adjacent wards and rooms in permanent occupancy.

In the following table are given the lead thicknesses required to ensure that the maximum permissible level is not exceeded.

Quantity of Radium (0.5 mm. Pt screen)	Thickness of Lead to Give Weekly Maximum Permissible Dose at the Following Distances from the Source				
	20 cm.	50 cm.	1 meter	2 meters	5 meters
gm.	cm.	cm.	cm.	cm.	cm.
0.1	10.0	6.0	3.5	1.0	0
0.2	11.5	7.5	4.5	2.0	0
0.5	13.5	9.5	6.5	4.0	0.5
1.0	15.5	11.0	8.0	5.0	1.5
2.0	16.0	12.5	9.5	6.5	3.0
5.0	18.0	14.5	11.5	8.5	4.5
10.0	19.5	16.0	13.0	10.0	6.0

Data may very conveniently be represented in a nomogram showing amounts of radiation through lead barriers at different distances from the source.

RECOMMENDATIONS FOR INTERNATIONAL SUBCOMMITTEES ON RADIATION PROTECTION AND FOR CORRESPONDING NATIONAL COMMITTEES AND SUBCOMMITTEES

1. In order to facilitate the work of the International Commission on Radiological Protection, which has become so arduous that a single small committee cannot encompass the whole field, it is proposed to establish a number of subcommittees to carry out detailed studies in specialized fields between the International Congresses of Radiology. The chairmen of these subcommittees need not necessarily be chosen from the membership of the International Commission on Radiological Protection.

The subcommittees suggested are as follows:

(1) Permissible dose for external radiation.
(2) Permissible dose for internal radiation.
(3) Protection against roentgen rays generated at potentials up to 2 million volts.
(4) Protection against roentgen rays above 2 million volts, and gamma rays and beta rays.
(5) Protection against heavy particles, including neutrons and protons.
(6) Disposal of radioactive wastes; handling of radioisotopes.

2. It is further proposed that the International Commission on Radiological Protection recommend that all interested

countries establish, each for itself, a central national committee to deal with problems of radiation protection—such a central committee to have subcommittees matching those of the International Commission on Radiological Protection as closely as their circumstances permit.

3. So far as possible, members of the International subcommittees should be selected from the corresponding subcommittees of the various national committees.

4. On matters of policy and formal agreements, communication will be from the central national committee to the International Commission. It is, however, recommended that direct communication on technical matters may be conducted between the corresponding national and international subcommittees.

PROPOSED RULES GOVERNING THE SELECTION AND WORK OF THE INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION

1. (a) The International Commission on Radiological Protection (I.C.R.P.) shall be composed of not more than twelve members. The selections shall be made by the International Executive Committee (I.E.C.) from a list of nominations submitted by the national delegations and by the International Commission on Radiological Protection itself. Members of the I.C.R.P. shall be chosen on the basis of their recognized activity in the fields of Radiology, Radiation Protection, Physics, Biology, Genetics, Biochemistry and Biophysics, without regard to nationality.

(b) The members of the I.C.R.P. shall be selected during one International Congress to serve through the succeeding Congress. Not less than two but no more than four members of the I.C.R.P. shall be changed at each Congress. In the intervening period a vacancy caused by conditions beyond the control of the I.E.C. shall be filled on the recommendation of the I.C.R.P.

(c) In the event of a member of the I.C.R.P. being unable to attend the I.C.R.P. meetings, a substitute may be selected by the I.C.R.P. as a temporary replacement. Such a substitute member shall not have voting privileges at the meetings unless specifically authorized by the I.E.C.

(d) The I.C.R.P. shall be permitted to invite individuals to attend its meetings to give special technical advice. Such persons shall not have voting privileges, but may ask permission to have their opinion recorded in the minutes.

2. The continuance of the policies and records of the I.C.R.P. shall be in the hands of a Secretary of the I.C.R.P. elected by the I.C.R.P. from among its regular members and subject to the approval of the I.E.C.

3. The I.C.R.P. shall familiarize itself with progress in the whole field of radiation protection. The Secretary shall be responsible for the preparation of a program to be submitted to the Commission for discussion at its meetings. Preliminary reports shall be prepared and circularized to all members of the I.C.R.P. and other specially qualified individuals at least six months before the meeting of the Congress.

4. The Chairman shall be elected by the I.C.R.P. six months in advance of the Congress. The choice shall not be limited to the members of the I.C.R.P. or to the country in which the Congress is held. Such a Chairman shall be a member of the I.C.R.P. *ex officio*, but for the period of the Conference only. Meetings between Congresses shall be presided over by the Secretary or other member selected by the I.C.R.P.

5. Decisions of the I.C.R.P. shall be decided by a majority vote, with the Chairman casting the deciding vote in case of a tie. A minority opinion may be appended to the minutes of a meeting if so desired by any member and upon his submission of same in writing to the Secretary.

L. S. Taylor, Acting Secretary
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National Bureau of Standards
Washington 25, D. C.

SUPPLEMENT ON MAXIMUM PERMISSIBLE AMOUNTS OF RADIOACTIVE ISOTOPES

INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION (JULY, 1950)

Report Prepared by Members of the International Commission on Radiological Protection as Follows:

E. Rock Carling, *Chairman*, Great Britain; L. S. Taylor, *Acting Secretary*, United States; W. Binks, Great Britain; E. L. Chérigié, France; A. J. Cipriani, Canada; R. G. Jaeger, Germany; W. V. Mayneord, Great Britain; R. R. Newell, United States; R. Sievert, Sweden

THE International Commission on Radiological Protection finds that, at present, it is not in a position to make firm recommendations regarding the maximum permissible amounts of radioactive isotopes that may be taken into, or retained in the body. It is possible, however, on the basis of the general principles set forth in "International Recommendations on Radiological Protection," as revised by I.C.R.P. at the Sixth International Congress of Radiology, July, 1950, to make reasonable calculations of the maximum permissible amounts of several of the more important radioactive isotopes.

In the meantime the I.C.R.P. draws attention to the following data on maximum permissible exposures to radioactive isotopes *for occupational workers*, presently used in the United States, Canada and the United Kingdom. The radioactive isotopes can enter the body either by inhalation, or by ingestion. Accordingly figures are also given for the maximum permissible levels (m.p.l.) of various isotopes in air and in liquid media.

Ra^{226}.

Clinical observations on chronic radium poisoning in man indicates that the most serious effects are anemia and damage to bone, including osteogenic sarcoma. Both effects appear to have a threshold of the order of 1 μc. fixed in the skeleton. Accordingly it is accepted that:

(a) *The maximum permissible amount of radium fixed in the body is 0.1μc.*

(b) *For radium appearing in the atmosphere as a soluble aerosol, assuming that 25 per cent of the inhaled amount is absorbed and that 25 per cent of the absorbed amount is retained with a mean life of about 10^4 days, the maximum concentration in air for soluble compounds is 8×10^{-12}μc./cc.*

(c) *If radium enters the body through liquid media, assuming 10 per cent of the ingested amount is retained with a mean life of about 10^4 days, the maximum permissible concentration of the liquid is 4×10^{-8} μc./cc.*

Pu^{239}.

On the basis of the relative biological effects of plutonium and radium, as observed in animal experiments, it is accepted that:

(a) *The maximum permissible amount of Pu^{239} fixed in the body is 0.04 μc.*

For soluble compounds of plutonium in the atmosphere, it is estimated that 10 per cent of the inhaled material is absorbed, with a mean life of 10^4 days. The maximum permissible concentration in air is, therefore, 2×10^{-12}μc./cc.

For insoluble compounds, it is estimated that the mean life in the lung is 200 days. If the irradiation of the lungs by alpha rays were limited to the biological equivalent of 0.3 r per week, the corresponding concentration of the plutonium in air would be 7.5×10^{-12}μc./cc. In view of the possibility of the transference of some of the insoluble material from the lungs to the skeleton, it is suggested that:

(b) *The maximum permissible concentra-*

tion of Pu^{239} in air is $2\times10^{-2}\mu c./cc.$, for soluble and insoluble compounds.

(c) *For Pu^{239} in liquid media, assuming that 0.1 per cent of the ingested amount is retained in the skeleton with a mean life of 10^4 days, the maximum permissible concentration is $1.5\times10^{-6}\mu c./cc.$*

Sr^{89} and Sr^{90} ($+Y^{90}$).

On the basis of the observed relative biological effects of Sr^{89} and Ra on animals, it is accepted that:

(a) *The maximum permissible amount of Sr^{89} in the body is 2.0 μc.*

Since the combined disintegration energy of the $Sr^{90}+Y^{90}$ pair is twice that of Sr^{89}, the maximum amount of Sr^{90} which can be permitted in the body is only one-half that of Sr^{89}. Accordingly:

(b) *The maximum permissible amount of Sr^{90} in the body is 1.0 μc.*

If strontium is assumed to behave like radium as regards uptake, then

(c) *For Sr^{90} in air, assuming that 25 per cent of the inhaled amount is absorbed and 25 per cent of the absorbed amount is retained with a mean life of about 15 years, the maximum permissible concentration is $2\times10^{-10}\mu c./cc.$*

(d) *For Sr^{90} in liquid media, assuming 10 per cent of the ingested amount is retained with a mean life of about 15 years the maximum permissible concentration is $8\times10^{-7}\mu c./cc.$*

Natural Uranium.

As the specific activity of natural uranium is so low, it is considered that the hazards arising from its use are mainly chemical.

Po^{210}.

Although polonium is not a bone-seeking isotope, some data exist on its toxicity relative to radium in animals. On this basis, it is accepted that:

The maximum permissible amount of Po^{210} in the body is 0.005 μc.

H^3.

It is assumed that tritium will be encountered in chemical forms in which free exchange takes place with ordinary hydrogen in the aqueous vapor in the lungs. If the mean energy of the beta radiation is 5.5 kv., a concentration of 0.14 μc. per gram of tissue will result in the biological equivalent of 0.3 r per week. The mean life of H^3 in the body is taken to be 10 days. A concentration of 0.14 μc./gram of tissue corresponds to 10 mc. uniformly distributed in the 70 kg. of the Standard Man. It is, therefore, accepted that:

(a) *The maximum permissible amount of H^3 in the body is 10 mc.*

(b) *The maximum concentration of H^3 in air, based on a permissible daily intake of 1 mc. and complete absorption in the lungs, is $5\times10^{-5}\mu c./cc.$*

(c) *The maximum concentration of H^3 in liquid media, based on a permissible daily intake of 1 mc., and complete absorption in the body, is 0.4 μc./cc.*

C^{14} (as CO_2 in air).

A rate of energy absorption biologically equivalent to 0.3 r per week would be produced by 0.014 μc. of C^{14} per gram of tissue. If the highest proportion of carbon in any tissue is 50 per cent then the maximum permissible concentration of C^{14} in carbon in the body is 0.028 μc. per gram of carbon. The postulated route of entry of C^{14} into the body is via the alveoli of the lungs, and the isotopic concentration in the alveolar air which must therefore be limited to 0.028 μc. per gram of carbon. Since alveolar air contains 5.5 per cent by volume of carbon dioxide, the maximum permissible concentration of C^{14} in the CO^2 of the alveolar air is about $1\times10^{-6}\mu c./cc.$

Accordingly:

The maximum permissible concentration of C^{14} as carbon dioxide in air is $1\times10^{-6}\mu c./cc.$

Na^{24}.

The energy (beta and gamma) absorbed

in the body per disintegration of Na^{24} is estimated to be 2.7 mev. Since sodium is uniformly distributed throughout the body:

(a) *The maximum permissible amount of Na^{24} in the body, corresponding to a dose rate biologically equivalent to 0.3 r per week, is 15 μc.*

Since biological excretion may be neglected in comparison to the radioactive decay, for which the mean life is 0.8 day:

(b) *For Na^{24} in liquid media, the maximum permissible concentration, assuming complete absorption, is 8×10^{-3} μc./cc.*

P^{32}.

Experimental and clinical data in man show that at times of the order of the mean life of P^{32}, i.e. about 20 days, the concentration of P^{32} in red bone marrow reaches a value only about three times the average concentration for the whole body. As most of the P^{32} is still diffused throughout the body, a dose rate biologically equivalent to 0.3 r per week in the critical tissue (red bone marrow) is therefore produced by a total quantity of approximately 25 μc. of P^{32} in the whole body. In order to allow for the possible occurrence of higher local concentrations in bone marrow:

(a) *The maximum permissible amount of P^{32} in the body is 10 μc.*

(b) *The maximum permissible concentration of P^{32} in liquid media assuming that 100 per cent is absorbed and that the biological excretion can be neglected in comparison to the radioactive decay is 2×10^{-4} μc./cc.*

Co^{60}.

Making the assumption that all the cobalt which is absorbed is deposited in the liver and that the effective energy in the liver is 1.3 mev. per disintegration, the amount of Co^{60} to give a dose rate biologically equivalent to 0.3 r per week is 1 μc. It is, therefore, accepted that:

(a) *The maximum permissible amount of Co^{60} in the body is 1 μc.*

(b) *The maximum permissible concentration of Co^{60} in liquid media, assuming 100 per cent absorption and a half-life in the liver of 20 days, is 1×10^{-5} μc./cc.*

I^{131}.

The energy absorbed in the thyroid gland per disintegration of I^{131} is estimated to be 0.27 mev., and so the amount of I^{131} in the gland to give a dose rate biologically equivalent to 0.3 r per week, is 0.18 μc., which would correspond to about 0.3 μc. in the body. It is, therefore, accepted that:

(a) *The maximum permissible amount of I^{131} in the body is 0.3 μc.*

(b) *The maximum permissible concentration of I^{131} in air assuming that 100 per cent is absorbed, that 20 per cent of the absorbed amount is deposited in the thyroid, and that biological excretion from the gland can be neglected in comparison to radioactive decay, is 3×10^{-9} μc./cc.*

(c) *The maximum permissible concentration if I^{131} in liquid media, assuming that 100 per cent is absorbed, that 20 per cent of the absorbed amount is deposited in the thyroid gland, and that biological excretion from the gland can be neglected in comparison to radioactive decay, is 3×10^{-5} μc./cc.*

All the preceding permissible amounts of isotopes refer to occupational exposure, and are summarized in the table.

	Ra^{226}	Pu^{239}	Sr^{89}	Sr^{90} $(+Y^{90})$	Po^{210}	H^3	C^{14} (as CO_2 in air)	Na^{24}	P^{32}	Co^{60}	I^{131}
Maximum permissible levels in body (μc.)	0.1	0.04	2.0	1.0	0.005	1×10^{4}	—	15	10	1	0.3 (0.18 in thyroid)
Effective mean life (days)	10^{4}	104	—	5000	—	10	—	0.8	20	20	12
Permissible daily deposition in body (μc.)	10^{-5}	4×10^{-5}	—	2×10^{-4}	—	1×10^{3}	—	20	0.5	0.05	0.015 (to thyroid)
Proportion absorbed via lungs and retained in body	0.06	0.1	—	0.06	—	1	—	—	—	—	0.2 (to thyroid)
Maximum permissible levels in air (μc./cc.)	8×10^{-12}	2×10^{-12}	—	2×10^{-10}	—	5×10^{-5}	1×10^{-6}	—	—	—	3×10^{-9}
Proportion retained from intestine	0.1	0.001	—	0.1	—	1	—	1	1	1	0.2
Maximum permissible levels in liquid media (μc./cc.)	4×10^{-8}	1.5×10^{-6}	—	8×10^{-7}	—	0.4	—	8×10^{-3}	2×10^{-4}	1×10^{-5}	3×10^{-5}

APPENDIX I

Standard Man

(a) *Mass of Organs*

Organs	Grams
Muscles	30,000
Skeleton, Bones	7,000
Red marrow	1,500
Yellow marrow	1,500
Blood	5,000
Gastrointestinal tract	2,000
Lungs	1,000
Liver	1,700
Kidney	300
Spleen	150
Pancreas	70
Thyroid	20
Testes	40
Heart	300
Lymphoid tissue	700
Brain	1,500
Spinal cord	30
Bladder	150
Salivary glands	50
Eyes	30
Teeth	20
Prostate	20
Adrenals	20
Thymus	10
Skin and subcutaneous tissues	8,500
Other tissues and organs not separately defined	8,390
Total Body Weight	70,000

(b) *Chemical Composition*

Element	Proportion Per cent	Approximate mass in grams in the body
Oxygen	65.0	45,500
Carbon	18.0	12,600
Hydrogen	10.0	7,000
Nitrogen	3.0	2,100
Calcium	1.5	1,050
Phosphorus	1.0	700
Potassium	0.35	245
Sulphur	0.25	175
Sodium	0.15	105
Chlorine	0.15	105
Magnesium	0.05	35
Iron	0.004	3
Manganese	0.0003	0.2
Copper	0.0002	0.1
Iodine	0.00004	0.03

The figures for a given organ may differ considerably from these averages for the whole body. For example, the nitrogen content of the dividing cells of the basal layer of skin is probably nearer 6 per cent than 3 per cent.

(c) *Applied Physiology*

Average data for normal activity in a temperate zone.

(i) *Water balance*

Daily Water Intake

In food (including water of oxidation)	1.0 liter
As fluids	1.5 liter
	2.5 liters

Calculations of maximum permissible levels for radioactive isotopes in water have been based on the total intake figure of 2.5 liters per day.

Daily Water Output

Sweat	0.5 liter
From lungs	0.4 liter
In feces	0.1 liter
Urine	1.5 liters
	2.5 liters

Total Water Content of Body 50 liters

(ii) *Respiration*

Area of Respiratory Tract

Respiratory interchange area	50 m^2
Non-respiratory area (upper tract and trachea to bronchioles)	20 m^2
Total	70 m^2

Respiratory Exchange

Physical Activity	Hours per Day	Tidal Air (liters)	Respirations per Minute	Volume per 8 Hours (m^3)	Volume per Day (m^3)
At work	8	1.0	20	10	20
Not at work	16	0.5	20	5	

Carbon Dioxide Content (by Volume) of Air

Inhaled air (dry, at sea level)	0.03%
Alveolar air	5.5%
Exhaled air	4.0%

(iii) *Retention of particulate matter in the lungs*

In those cases where specific data are lacking, the convention has been adopted that 50 per cent of any aerosol reaches the alveoli of the lungs. If the particles are soluble, they have been considered to be completely absorbed; if insoluble, then the 50 per cent amount has been regarded as retained for 24 hours, after which only half of it, i.e., 25 per cent of the inhaled amount, is retained *in situ* indefinitely.

(d) *Duration of Exposure*

(i) *Duration of occupational exposure*

The following figures have been adopted in calculations pertaining to occupational exposure:

8 hours per day
40 hours per week
50 weeks per year

(ii) *Duration of "lifetime" for non-occupational exposure*

A conventional figure of 70 years has been adopted.

APPENDIX II

Relative Biological Efficiency

The relative biological efficiency of any given radiation has been defined by comparison with the gamma radiation from radium filtered by 0.5 mm. of platinum. It has been expressed numerically as the inverse of the ratio of the dose of the two radiations (in ergs per gram of tissue) required to produce the same biological effect under the same conditions. It has been assumed, for purposes of calculation, that the relative biological efficiency of a given radiation is the same for all effects mentioned in the Introduction, with the single exception of gene mutations.

The following values have been adopted:

Radiation	Relative Biological Efficiency
Gamma rays from radium (filtered by 0.5 mm. Pt)	1.0
Roentgen rays of energy 0.1 to 3.0 mev.	1.0
Beta rays	1.0
Protons	10
Fast neutrons of energy not greater than 20 mev.	10
Alpha rays	20

The effective figure for slow neutrons should be derived in any given case from an evaluation of the separate contributions to the biological effect by protons arising from the disintegration of the nitrogen nuclei and by gamma rays arising from the capture of neutrons by hydrogen nuclei.

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DEPARTMENT OF TECHNIQUE

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A SIMPLE MANUAL CASSETTE CHANGER FOR MULTIPLE EXPOSURES IN ANGIOCARDIOGRAPHY*†

By ALBERT D. KISTIN, M.D.

WASHINGTON, D. C.

THE recognition of the diagnostic value of angiocardiography by the technique of Robb and Steinberg[5] has led to the development of a number of devices for obtaining multiple exposures in rapid succession.[1–4,6–15] These are complex and expensive, or are suitable for making roentgenograms with the subject in either the vertical or horizontal position but not in both. This is a description of a simple inexpensive device which uses standard 14 by 17 inch cassettes. It may be used with the patient in either the upright or recumbent position, and it provides exposures at approximately one and one-half second intervals. This cassette changer is a modification of one described by Neuhauser and Jennings.[4]

In Figure 1 the construction of the changer is illustrated, and in Figure 2 its use in the vertical and horizontal positions is shown. A board the size of the cassettes is mounted on four metal cylinders which carry springs. A lever pulls the board back to load the cassettes, and there is a catch to hold the lever as the cassettes are being loaded. The cylinders move through metal sleeves fastened to the back of the box. The diameter of the sleeves is only slightly greater than that of the cylinders so that, as the latter are pulled back by the lever, the springs carried on them become compressed. The cassettes are loaded in front of the moving board (*above* the board when the subject is in the recumbent position). Release of the lever presses the board against the cassettes. The floor over which the cassettes slide forward in the vertical position is made of smooth metal. As each exposure is made, the foremost (or topmost) cassette is pulled out and the spring tension snaps the next cassette into place. The floor of the box, the outside surfaces of the metal cylinders, and the joints of the lever are well lubricated before use.

Ordinary cassettes are used to the sides of which metal handles have been screwed and which have been protected by lead backings. A sheet of lead, one-sixteenth of an inch thick is placed between the back of the cassette and the felt backing. To insert the lead sheet, the felt backing and its attached intensifying screen are carefully stripped away from the back of the original cassette, and both the lead and the felt backing can then be kept in place with ordinary glue. The ends of the metal clasps on the back of the cassette should extend well into the side grooves when the cassette is closed; otherwise the jolting and pulling may work a clasp loose and jam the rapid changing. We experienced this difficulty and remedied it by using cassettes with secure clasps.

The springs are the most important part of the changer. They must have adequate tension to carry the cassettes forward (or upward), and yet at the same time the tension must not be so excessive as to

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interfere with rapid removal of the cassettes. Each of our cassettes with the lead sheet inserted weighs about 13 pounds. We usually use a series of eight exposures. The springs used for roentgenograms of subjects in the vertical position are made of 11 gauge spring steel wire. They have a free length of 18 inches, their outside diameter is 2 inches, and there are 18 coils over the entire length of spring. To make roentgenograms of subjects in the horizontal position, more spring tension is necessary to overcome the effect of gravity. Two of the springs described above, diagonally opposite each other, are then replaced by heavier springs made of 7

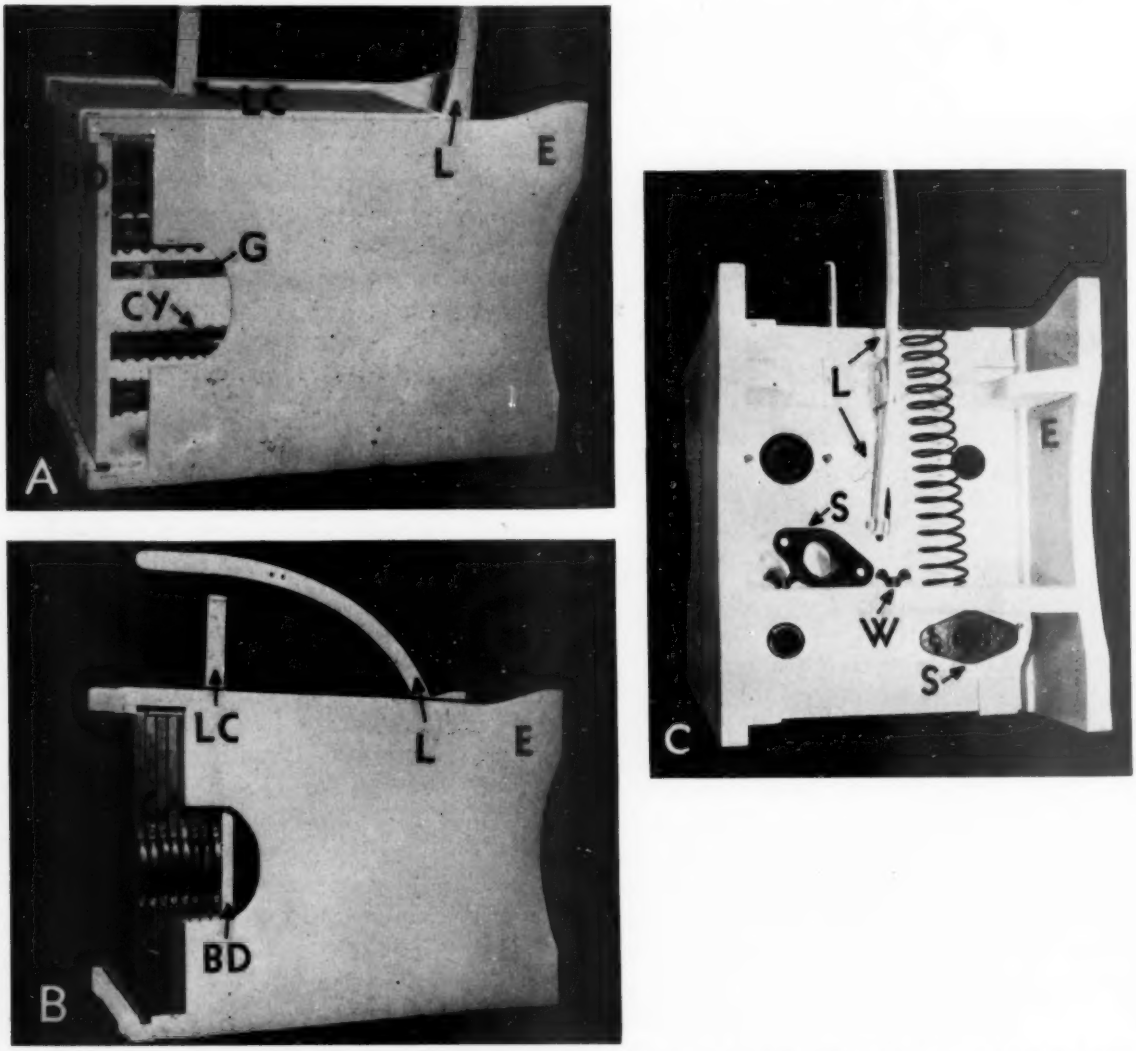

Fig. 1. Cassette changer. (*A*) Side and partly front and top view, unloaded. (*B*) Side and partly front view, cassettes in place. (*C*) Rear view. BD, movable board; CA, cassettes with attached handles; CY, one of the four metal cylinders mounted on movable board and carrying springs; E, extension which serves as leg for the cassette changer when making angiocardiograms in the horizontal position; G, guide attached to center of movable board in front and to lever behind; L, lever for pulling back movable board to load cassettes; LC, lever catch; S, metal sleeve; W, wing bolt for mounting metal sleeve. The rear view (*C*) shows a heavy spring removed and a lighter spring almost completely inserted, upper left. The metal sleeve and wing bolts, lower right, are in place; those of upper left are shown removed. For the metal cylinders, upper right and lower left, the sleeves were mounted on the inside of the box, since it was found necessary to replace only two of the springs in changing from vertical to horizontal position.

gauge spring steel wire. The interchange of the springs is made within a few minutes; two of the metal sleeves through which the cylinders move are each held in place on the outside of the back of the changer by two thumb screws. These heavier springs are 18 inches long, their outside diameter is $2\frac{3}{8}$ inches and there are 22 coils over the entire length of spring.

The satisfactory changing of the cassettes requires a minimum of practice and teamwork. One technician controls the exposures with a stop-watch, while another technician pulls the cassettes. Our method was briefly as follows. As the physician injecting the diodrast gives the subject the command, "Breathe *in*," he starts the injection on *in*, and the technician simultaneously starts timing. The latter makes exposures at predetermined times, and with each exposure he calls, "Click." This is the signal for the other technician to immediately pull a cassette and wait for the next "click." The timing is, of course, flexible. Either a rapid series of exposures at approximately one and one-half second intervals may be obtained, or staggered timing may be used, as, for example, a series of exposures early after the injection followed by any desired pause and then another series of exposures. The technician pulling the cassettes lays them face downward on a blanket, either on the floor when the horizontal position is used, or on a table when the vertical position is used. This technician and the physician giving the injection are protected by portable lead screens. In some positions a screen is inadequate protection for the physician and a lead apron is preferable.

We used a Potter-Bucky diaphragm that was available in the roentgenology department for routine work. In the vertical position provision was made to hold this in place, in a stand on which the changer is set. In the horizontal position the diaphragm holder is fastened to the table top with two C-clamps. Aside from these two clamps there should be no direct pressure on the Potter-Bucky diaphragm holder. The table top with the subject on it should be just clear of contact with the face of the Potter-Bucky holder. Direct pressure on the holder which we used prevented shifting of the diaphragm.

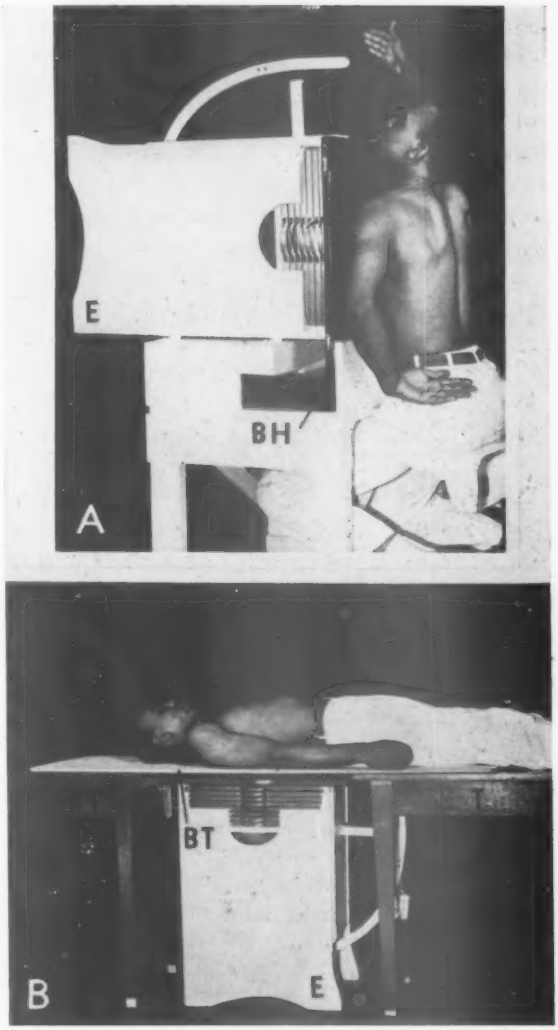

FIG. 2. (*A*) Use of cassette changer in vertical position. (*B*) Use of cassette changer in horizontal position. BH, Potter-Bucky diaphragm holder; BT, board top placed between tables; E, extension which serves as leg for cassette changer when making angiocardiograms in the horizontal position; T, table on either side of cassette changer.

This changer has received considerable use over a period of ten months and has proved entirely satisfactory. Exposures at about one and one-half second intervals are adequate for diagnostic purposes. With a smoothly operating team, we have made

good exposures at intervals of one second. There is a certain amount of vibration during the changing but most of the vibration seems to occur between exposures. Moreover, the motion of the cassettes due to vibration is in the film-tube axis. Blurring is more likely with cassette changers where the motion of the cassettes during changing is across this axis. Using the factors, 300 ma., 75 to 95 kv. and 1/6 to 1/10 sec. our roentgenograms are quite sharp.

In most cases it is not necessary to employ the entire 14 by 17 inch area for angiocardiograms, and a changer employing somewhat smaller cassettes might be suitable. In a few cases, however, the larger size proved valuable. One example is a case of pulmonary arteriovenous aneurysm of the right middle lobe in which a number of previously unsuspected smaller aneurysms were detected at the periphery of the left lower lung field. Another example is a case of coarctation of the aorta in which distinct collateral vessels in both the axillary and subscapular regions could be demonstrated in a single left oblique view.

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Vol. 65, No. 4

DURAL VENOUS SINOGRAPHY*

A METHOD OF VISUALIZATION OF THE SAGITTAL DURAL SINUS AND ITS TRIBUTARIES BY DIRECT INJECTION OF DIODRAST

PRELIMINARY REPORT

By MICHAEL SCOTT, M.D.

PHILADELPHIA, PENNSYLVANIA

IT MAY be advantageous at times for the clinician to know whether the sagittal dural sinus and its tributaries are obstructed by a thrombus or distorted or occluded by a parasagittal tumor, such as a meningioma.

This information can be obtained during the venous phase of a percutaneous or open carotid arteriogram. However, the venous filling is frequently inadequate during arteriography and the following method is suggested when arteriography gives insufficient information, or is not feasible for technical reasons, and particularly where the clinician is primarily interested in the venous dural sinuses and their tributaries.

Frenckner[1] (1936) was the first to attempt direct visualization of the transverse and jugular sinus by direct injection. He trephined 5 cm. above the external occipital protuberance and injected 35 per cent parabrodil directly into the sagittal sinus in 3 cases of suspected jugular sinus thrombosis. The method did not permit visualization of the middle third of the sagittal sinus, which is the portion involved in parasagittal tumors and which produces profound neurologic disturbances if obstructed or ligated.

The following method was devised by the writer[2] (1948) and gave satisfactory visualization of the sagittal sinus and its tributaries in 3 infants. In 1 case of amyotonia congenita an associated obstruction of the middle third of the sagittal sinus was visualized, together with the collateral cerebral venous shunt which by-passed the obstruction to the lateral sinus (Fig. 2). The remaining 2 cases (subdural hematomas) showed normal sinograms (Fig. 3).

TECHNIQUE

1. In infants with open fontanelles,† under a general anesthetic a 2.5 cm. coronal incision is made within the hair line across the anterior portion of the anterior fontanelle (Fig. 1). The scalp and periosteum is dissected from the dura and the sagittal sinus is exposed for a distance of at least

FIG. 1. Incision for direct exposure of the sagittal sinus.

† The procedure must be done carefully since the needle could perforate the sinus and produce a subdural hematoma. The author therefore insists upon the following precautions: (a) All infants or potentially uncooperative patients should be examined under a general anesthetic to avoid sudden jerking of the head. (b) The procedure should *always* be done through an open incision with the sinus adequately exposed for a distance of at least 2 cm. The needle should be inserted into the mid-portion of the sinus and never deeper than 4 mm.

Ray and associates[3] have recently suggested inserting a small polyethylene catheter into the sagittal sinus. This obviates the danger of perforation of the sinus by a needle and is a definite improvement in technique.

* From the Department of Neurosurgery, Temple University Hospital and Medical School, Philadelphia, Pennsylvania.

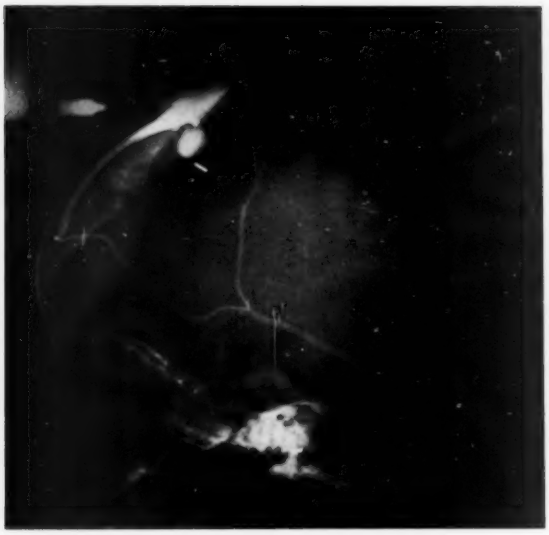

Fig. 2. Case of amyotonia congenita, infant aged seven months. Eight cubic centimeters of 35 per cent diodrast injected into sagittal sinus through an incision across anterior fontanelle. The sinus is occluded posterior to the fontanelle. The dye has thus filled in a retrograde manner the anterior third of the sagittal sinus and is by-passing the obstruction through collateral veins running to the transverse sinus.

2 cm. An 18 gauge (1¼ inch) short bevel needle is luerlocked to a 10 cc. syringe filled with 35 per cent diodrast.* The patient is properly positioned on the roentgen table. The needle is carefully inserted 2 to 4 millimeters into the mid-portion of the sinus and, when blood is obtained, 8 to 10 cc. of the dye is rapidly injected. During the injection of the last 2 cc. appropriate lateral exposures are made.† If the anteroposterior view is desired an additional 8 to 10 cc. can be injected. Stereoscopic views would necessitate four separate injections. After the injection the needle is removed rapidly and a tiny pledget of gelfoam is pressed over the needle puncture, the incision is then closed with three or four silk sutures.

2. In children with closed fontanelles or in adults, a similar incision is made. An opening is made in the bone just lateral to the midline with a Hudson burr and the opening enlarged by a rongeur to expose the sagittal sinus. The technique is the same except that local anesthesia could be used in adults and 12 to 14 cc. of the dye injected at each exposure.

* Allergic tendencies should be ruled out by adequate history and diodrast sensitivity tests.

† Horizontal ray for lateral views and vertical ray for anteroposterior views. The following factors were used: 65 kilovolts; 100 milliamperes; ½ second; 46 inches target film distance.

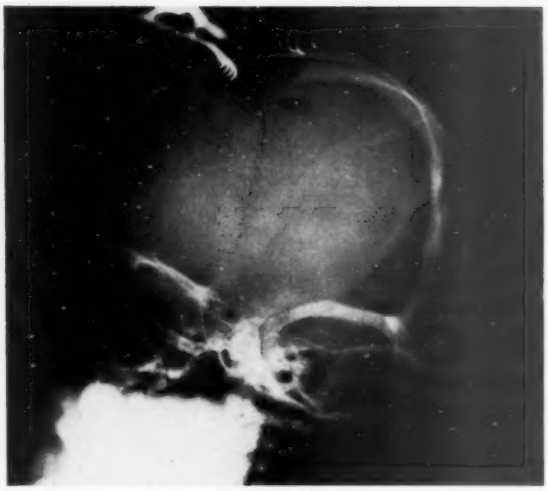

Fig. 3. Normal sagittal sinovenogram. Note excellent filling distal to injection of the sagittal sinus, torcular Herophili and both lateral and sigmoid sinuses.

Conclusions

A method is described for visualizing the sagittal sinus and its tributaries by the direct injection of 35 per cent diodrast into the anterior third of the sagittal sinus. Where the venous phase of arterial angiography proves unsatisfactory or is not feasible, this method should be of help in determining obstruction or distortion due to thrombosis or parasagittal tumors.

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Fifty-second Annual Meeting: Shoreham Hotel, Washington, D. C., September 25–28, 1951.

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Thirty-third Annual Meeting: Hotel Claridge, Atlantic City, N. J., June 7–9, 1951.

EDITORIALS

THE ANNUAL MEETING OF THE AMERICAN RADIUM SOCIETY

THE Thirty-Third Annual Meeting of the American Radium Society will be held at the Claridge Hotel, Atlantic City, New Jersey, June 7, 8 and 9, 1951. An interesting and instructive program has been outlined for the two and a half day meeting. It is urged that all those wishing to attend, and let me say that visitors are most welcome, should make their reservations immediately.

The Preliminary Program of the American Radium Society is published in this issue of the JOURNAL.

A study of the program indicates an effort on the part of the Society to consider the indications and end results of the various forms of cancer therapy, a briefing in the advances that one cannot afford to miss in this day and age as constant improvements are being made.

A well rounded symposium on tumors of the head and neck is indeed timely. The various means of attacking the problems indicate that there is no set or proved method of treating malignant conditions in this region, and it further indicates that with our knowledge to date each patient requires careful consideration to determine the proper and best approach to his individual problem.

Tumors of the head and neck, as common as they are, present a real challenge to the young radiologist and surgeon who must, in many instances, make a choice resulting in either life or death to the individual so afflicted. In a few training centers the training is, unfortunately, entirely surgical, while in others the primary training is almost entirely radiologic. In order to broaden the scope of training and to bring out other approaches to the treatment of malignant disease, it is timely to have a group who can conservatively and wisely present the various forms of treatment and state in an authoritative way their approach to the problems and their results, and thus give us an opportunity to treat our patients in the best possible manner.

The use of biochemicals in the treatment of cancer is, of course, not new, but each year new drugs are tried and, regardless of the results, they increase our knowledge. A series of papers are to be presented in order to bring us up to date on the treatment of malignant disease by biochemical means and also by the use of colloidal radioactive isotopes.

The highlight of the program will, as usual, be the Janeway Lecture which will be presented on Friday afternoon, June 8, 1951. This year the Society and guests will have the plesaure of hearing Dr. H. Dabney Kerr, Iowa City, Iowa, who needs no introduction. It is well to remember that men who are chosen to give this lecture have spent many years of hard work in radiation therapeutics before receiving the highest award of the Society. If one reviews the list of those who have previously given the Janeway Lecture he will find the stepping stones to better therapy year after year.

Again, all are invited to attend this meeting. It is hoped that through listening and and discussion we may all gather a few pearls to take home.

HUGH F. HARE, M.D.
President-Elect
American Radium Society
The Lahey Clinic
Boston, Massachusetts

JOHN B. JACKSON
1876–1950

THE profession of radiology suffered a true loss in the passing of Dr. John B. Jackson, of Kalamazoo, Michigan, on November 2, 1950. This prominent physician and radiologist was for twenty-two years an associate of the late Dr. A. W. Crane.

Born on June 11, 1876, near Kalamazoo, Michigan, Dr. Jackson began practice in 1905 following an internship at St. Mark's Hospital, Salt Lake City, Utah. Previous to this he had studied at the University of Michigan and the Rush Medical College,

receiving his degree from the latter college in 1903.

Early experience in the teaching profession as a high school principal and school superintendent permitted his gaining fundamental knowledge in the art of teaching. This faculty of being a teacher by example was an outstanding accomplishment in the later life of this exceptional man.

As a city health officer, he established the first fresh-air cottage for tuberculosis treatment in southwestern Michigan. He also served as president of the Kalamazoo Civic Improvement League. Further civic contributions and interests are reflected by his past presidency of the Family Service Center board and of the Kiwanis Club. He was an active member of the Outlook Club, Torch Club and the Medical Journal Club. He was medical adviser for the military district of thirty-five counties during World War I.

Dr. Jackson's professional honors included presidency of the Michigan State Medical Society in 1926 and of the Kalamazoo Academy of Medicine in 1918. He served as Chief of Staff of Bronson Methodist Hospital for many years after the hospital's organization. His interest in tuberculosis prompted an active participation in the American Trudeau Society. He was a fellow of the American College of Radiology, the American College of Physicians and of the American Medical Association. He held membership in the American Roentgen Ray Society and the Radiological Society of North America.

Well grounded in the branches of internal medicine and pediatrics, Dr. Jackson became associated in the practice of radiology with Dr. Crane in 1915. The significance and importance of basic medical training for all radiologists was readily appreciated by this master internist. His versatility as an outstanding physician was recognized by all who knew him. This achievement permitted Dr. Jackson to be an early friend and counselor of all younger physicians entering the community.

His scientific activities also covered medical writings on a variety of subjects in their relation to the developing science of radiology. These were mostly written during the 1920's.

One cannot complete this tribute without referring to Dr. Jackson's activity as a church man. He was a member of the Episcopal Church vestry for many years and was senior warden of the Church. Everyone knew him as a deeply religious man and one whose faith was unshaken.

Dr. Jackson is survived by his wife, two daughters and a son. The son is a practicing surgeon.

As these words in memory of Dr. Jackson are closed, the sense of heavy loss in the passing of one who was at once a colleague, a teacher, and a friend, is tempered by the example of courage, kindliness and wisdom that such a life as his was given to those of us who knew and loved him.

R. C. Hildreth, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Shoreham Hotel, Washington, D.C., Sept. 25–28, 1951.

American Radium Society
Secretary, Dr. J. E. Wirth, U. S. Marine Hospital, Baltimore, Md. Annual meeting: Hotel Claridge, Atlantic City, N. J., June 7–9, 1951.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y., Annual meeting: 1951, to be announced.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6.

Section on Radiology, American Medical Association
Secretary, Dr. P. C. Hodges, 950 E. 59th St., Chicago, Ill. Meets Atlantic City, N. J., June 11–15, 1951.

Alabama Radiological Society
Secretary, Dr. W. W. Anderson, Tuscaloosa, Ala. Meets time and place Alabama State Medical Association.

Arizona Association of Pathologists and Radiologists
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Atlanta Radiological Society
Secretary, Dr. T. F. Leigh, Emory Univ. Hospital, Emory University, Ga. Meets monthly, except during three summer months, on second Friday evening.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, Oct. through April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. B. D. Braun, 6 N. Michigan Ave., Chicago 2, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

Cincinnati Radiological Society
Secretary, Dr. E. C. Elsey, 927 Carew Tower, Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. J. R. Hannan, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
Secretary, Dr. Paul E. RePass, 306 Republic Bldg., Denver 2, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday Oct. and April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. J. C. Cook, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. T. H. Lipscomb, 30 W. Beaver St., Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. R. C. Pendergrass, Americus, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Greater Cincinnati Radiological Society
Secretary, Dr. Lawrence Gibboney, Carew Tower, Cincinnati 2, Ohio. Meets first Monday of each month.

Greater Miami Radiological Society
Secretary, Dr. T. M. Berman, 350 Lincoln Rd., Miami Beach, Florida. Meets last Wednesday of each month at 8:00 P.M. at Veterans Administration Regional Office.

Houston Radiological Society
Secretary, Dr. F. M. Windrow, 1205 Hermann Professional Bldg., Houston, Texas. Meets fourth Monday each month.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society.

Kansas Radiological Society
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

Kentucky Radiological Society
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

Kings County Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Wybren Hiemstra, 1414 S. Hope St., Los Angeles 15, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

* Secretaries of societies are requested to send timely information promptly to the Editor.

Maine Radiological Society
Secretary, Dr. C. F. Miller, Central Maine General Hospital, Lewiston, Maine.

Miami Valley Radiological Society
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

Michigan Association of Roentgenologists
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

Mid-Hudson Radiological Society
Secretary, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, Sept. to May.

Milwaukee Roentgen Ray Society
Secretary, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. L. A. Nash, 572 Lowry Medical Arts Bldg., St. Paul 2, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

Nebraska Radiological Society
Secretary, Dr. R. W. Blanchard, 1216 Medical Arts Bldg., Omaha, Nebr. Meets fourth Thursday of each month at 6 P.M. at Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. L. L. Robbins, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

New Hampshire Roentgen Ray Society
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

New York Roentgen Society
Secretary, Dr. J. L. Olpp, 49 Ivy Lane, Tenafly, N. J. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Radiological Society
Secretary, Dr. J. F. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

North Dakota Radiological Society
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

Northern California Radiological Club
Secretary, Dr. C. W. Wauters, 701 High St., Auburn, Calif. Meets at dinner last Monday, every second month, except June, July and August.

Ohio State Radiological Society
Secretary, Dr. E. C. Elsey, 927 Carew Tower, Cincinnati 2, Ohio.

Oklahoma State Radiological Society
Secretary, Dr. W. E. Brown, 21st & Xanthus, Tulsa 4, Okla. Three regular meetings annually.

Oregon Radiological Society
Secretary, Dr. C. T. Jessell, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

Pacific Northwest Radiological Society
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport. Annual meeting, May 18 and 19, 1951, at William Penn Hotel, Pittsburgh, Pa.

Philadelphia Roentgen Ray Society
Secretary, Dr. G. P. Keefer, American Oncologic Hospital, Philadelphia 4, Pa. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary Dr. E. J. Euphrat, 3500 Fifth Ave., Pittsburgh 13, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

Queens Roentgen Ray Society
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, Sept. to May.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Fred Zaff, 135 Whitney Ave., New Haven, Conn. Meets bimonthly on second Wednesday.

Radiological Section, District of Columbia Medical Society
Secretary, Dr. K. C. Corley, 1835 Eye St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, Jan., March, May, Oct. at 8:00 P.M.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of New Jersey
Secretary, Dr. Peter Gianquinto, 685 High St., Newark, N. J. Meets annually at Atlantic City at time of State Medical Society and mid-winter at Elizabeth, N. J.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. A. V. Winchell, 40 Meigs St., Rochester, N. Y. Meets monthly on last Monday from September through May, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Meets August 9, 10, 11, 1951, at Denver, Colorado.

St. Louis Society of Radiologists
Secretary, Dr D. S. Bottom, 510 S. Kingshighway, St. Louis, Mo. Meets fourth Wednesday each month, except June, July, August, and September.

San Diego Roentgen Society
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Tuesday at dinner.

Section on Radiology, California Medical Association
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. S. H. Fisher, 107 E. North St., Greenville, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Meets Houston, Texas, Jan. 18 and 19, 1952.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. R. C. Kiltz, 705 Medical-Dental Bldg., Everett, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

Wisconsin Radiological Society
Secretary, Dr. Irving I. Cowan, 425 E. Wisconsin Ave., Milwaukee 2, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
Secretary, Dr. M. A. Sisson, 450 Sutter St., San Francisco, 8, Calif. Meets Jan. to July, Lane Hall, Stanford Univ. Hospital; July to Dec. San Francisco Hospital.

Cuba, Mexico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86 Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. Jean Bouchard, Suite 305, 1555 Summerhill Avenue, Montreal 26, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. L. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. R. de G. Burnard, 170 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

South America

Asociacion Argentina de Radiologia
Secretary, Dr. Lidio G. Mocsa, Avda. Gral Paz 151, Córdoba, Argentina. Meetings held monthly.

Sociedad Argentina de Radiologia, Junta Central, Buenos Aires
Secretary, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Argentina de Radiologia, Filial del Litoral, Sede, Rosario
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

Sociedad Argentina de Radiologia, Filial del Sur, Sede, La Plata
President, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Centro, Sede, Cordoba
President, Prof. Dr. David L. Caro, Corro 86, Cordoba. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Norte, Sede, Tucuman
President, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

Sociedad Argentina de Radiologia, Filial de Cuyo, Sede, Mendoza.
President, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Colombiana de Radiologia
Secretary, Dr. Alberto Torres Focke, Av. 34, No. 17–34, Bogota, Colombia. Meets last Wednesday of each month.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Ceskoslovenská společnost pro röntgenologii a radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad. USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Societa Italiana di Radiologia Medica
Secretary Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

PRELIMINARY PROGRAM

American Radium Society

The following is the preliminary program which has been arranged for the Thirty-third Annual Meeting of the American Radium Society to be held at the Claridge Hotel, Atlantic City, New Jersey, Thursday, Friday and Saturday, June 7, 8 and 9, 1951.

Thursday Morning, June 7, 1951

9:00 Executive Session

9:30 Presidential Address. Leland R. Cowan, M.D., Salt Lake City, Utah.

Symposium on Head and Neck

9:50 An Evaluation of Preoperative Irradiation Combined with Dissection of the Lymph Nodes of the Neck. S. Gordon Castigliano, M.D., Philadelphia, Pa.

10:10 Salvage of Recurrent Carcinoma of the Larynx (Laryngopharyngectomy). John V. Blady, M.D. Philadelphia, Pa.

10:30 Interstitial Radium in the Treatment of Carcinoma of the Tongue. Theodore P. Eberhard, M.D., Philadelphia, Pa.

10:50 Surgical Neck Node Dissection in Carcinoma of the Head and Neck. Henry P. Royster, M.D., Philadelphia, Pa.

11:10 The Detection of Gastric Carcinoma by Photofluorographic Methods. Russell H. Morgan, M.D., Baltimore, Md.

11:30 The Roentgen Diagnosis and Follow-up of Hypopharyngeal Carcinomas. Dr. Solve Welin, Stockholm, Sweden. Discussion: Edith H. Quimby, Sc.D., New York, N.Y., and Franz J. Buschke, M.D., Seattle, Wash.

Thursday Afternoon, June 7, 1951

2:00 Roentgen Treatment of Sterility. Walter W. Williams, M.D., Springfield, Mass.

2:20 The End Results in Treatment of the Soft Somatic Tissues. George T. Pack, M.D., and Theodore Miller, M.D., New York, N. Y.

2:40 Cancer of the Esophagus: Its Surgical Management. W. L. Watson, M.D., New York, N. Y.

3:00 Resection of Solitary Metastasis to the Lung. J. Maxwell Chamberlain, M.D., New York, N. Y.

3:20 Abdominopelvic Lymph Node Dissections in Cancer of the Rectum and Distal Colon. Michael R. Deddish, New York, N. Y.
Movie: Dissection of the Pelvic Lymph Nodes. George T. Pack, M.D., New York, N. Y.

Friday Morning, June 8, 1951

9:30 Rotational Scanning of Breast Malignancies with Supervoltage Radiation. Hugh F. Hare, M.D., John G. Trump, Sc.D., and E. W. Webster, Sc.D., Boston, Mass.

9:50 Late Sequelae of Supervoltage Irradiation. Franz J. Buschke, M.D., Seattle, Wash.

10:10 Comparative Study of Various Irradiation Methods as Adjunct to Surgery

in Carcinoma of the Fundus Uteri. Traian Leucutia, M.D., Detroit, Mich.

10:30 Treatment of Carcinoma of the Gums with Low Intensity Radium Needles. Charles L. Martin, M.D., and Edward J. Craffey, M.D., Dallas, Tex.

10:50 Carcinoma of the Larynx Treated by 500 Kilovolt Roentgen Rays. J. Samuel Binkley, Los Angeles, Calif.

Friday Afternoon, June 8, 1951

SYMPOSIUM ON COLLOIDAL RADIOACTIVE ISOTOPES (GOLD OR CHROMIC PHOSPHATE)

2:00 Intraperitoneal Use for Advanced Ovarian Malignancy with Peritoneal Seeding and/or Ascites. Richard H. Chamberlain, M.D., Philadelphia, Pa.

2:40 Injection of Colloidal Isotopes for Pelvic Cancer. James F. Nolan, M.D., Los Angeles, Calif.

3:00 Irradiation of Cancer of the Uterine Cervix with Radioactive Cobalt 60 in Guided Aluminum and in Plastic Threads. J. L. Morton, M.D., William G. Myers, M.D., Allan C. Barnes, M.D., and George W. Callendine, Columbus, Ohio.

3:20 Complications Arising from Treatment of Cervical Carcinoma. A. N. Arneson, M.D., St. Louis, Mo., M. D. Bonebrake, M.D., Salem, Mo., and Alfred I. Sherman, M.D., St. Louis, Mo.

4:00 Janeway Lecture. H. Dabney Kerr, M.D., Iowa City, Iowa.

6:45 Banquet

Saturday Morning, June 9, 1951

9:30 The Treatment of Irradiation Damage to the Female Genitalia. Gray H. Twombly, M.D., New York, N. Y.

9:50 Treatment of Multiple Myeloma with Urethane. Ralph Jones, M.D., Philadelphia, Pa.

10:10 The Use of Triethylene Melamine: A Compound with Nitrogen Mustard-like Activity in the Treatment of Neoplastic Disease. David A. Karnofsky, M.D., New York, N. Y.

10:30 The End Results in the Treatment of Malignant Lymphoma with Special Reference to Hodgkin's Disease. John F. Hynes, M.D., Wilmington, Del.

10:50 Review of All Cases of Hodgkin's Disease: Symptoms, Methods of Treatment, Longevity, etc. William E. Howes, M.D., Brooklyn, N. Y.

11:10 Regional Administration of Nitrogen Mustard as an Adjunct to Radiation Therapy in the Treatment of Cancer. Calvin Klopp, M.D., Washington, D. C.

CONGRÈS DES MÉDECINS ELECTRORADIOLOGISTES

Congrès des Médecins Electroradiologistes will be held in Brussels, Belgium, from July 23–28, 1951, under the presidency of Professor Maisin. The general topic discussed will be the study of non-tuberculous chronic articular lesions. The Congress will include a section of radiobiology, radiodiagnosis, radiotherapy, electrotherapy and radiologic physics. The Secretariat of the Congress is at the Maison des Médecins, 54, Boulevard de Waterloo, Bruxelles, Belgium.

GREATER CINCINNATI RADIOLOGICAL SOCIETY

At a recent meeting of the Greater Cincinnati Radiological Society the following officers were elected for the year 1950–1951: *President*, Dr. Norman Adair; *Vice-President*, Dr. Archie Fine; *Secretary-Treasurer*, Dr. Lawrence Gibboney, all of Cincinnati.

GREATER MIAMI RADIOLOGICAL SOCIETY

At a recent meeting of the Greater Miami Radiological Society, the following officers were elected for the coming year: *President*, Dr. Frazier Payton, Miami; *Secretary*, Dr. Theodore M. Berman, Miami Beach.

HOUSTON RADIOLOGICAL SOCIETY

The Houston X-Ray Club was reorganized during 1950 and adopted the name of the Houston Radiological Society. The officers for 1951 are as follows: *President*, Dr. Palmer E. Wigby; *Vice-President*, Dr. Luther M. Vaughan; *Secretary*, Dr. Frank

M. Windrow; *Treasurer*, Dr. Harry Fishbein, all of Houston, Texas.

INDIAN RADIOLOGICAL ASSOCIATION

At a recent meeting of the Indian Radiological Association, Captain M. Mukherji, M.B., D.M.R.E. (Camb.), was elected President for the coming year. The Annual Congress of the Association was held in Calcutta, India, from February 12–15, 1951. The General Secretary of the Association is Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

PENNSYLVANIA RADIOLOGICAL SOCIETY

The Thirty-sixth Annual Meeting of the Pennsylvania Radiological Society will be held at the William Penn Hotel, Pittsburgh, Pennsylvania, on May 18 and 19, 1951.

The officers of the Pennsylvania Radiological Society serving for 1950–1951 are as follows: *President*, Dr. Edgar C. Baker; *President-Elect*, Dr. Maurice F. Goldsmith; *First Vice-President*, Dr. Joseph T. Danzer; *Second Vice-President*, Dr. D. Alan Sampson; *Secretary-Treasurer*, Dr. James M. Converse; *Editor*, Dr. Carl B. Lechner.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

The next annual meeting of the Rocky Mountain Radiological Society will be held on August 9, 10 and 11, 1951, at Denver, Colorado.

MEETINGS AT TEXAS MEDICAL CENTER

Several meetings of interest to scientists and physicians will be held at the Texas Medical Center, Houston, Texas, on April 20 and 21, 1951.

These will include the *Fifth Annual Symposium on Fundamental Cancer Research* of the University of Texas M. D. Anderson Hospital for Cancer Research. One half day will be devoted to selected papers on the subject of protein metabolism in cancer. The *Cancer Pathology Conference* of the University of Texas Postgraduate School of Medicine will be concerned primarily with breast cancer. Other types of tumors will be discussed, however. A *South Central Region Meeting of the College of American Pathologists*, with coparticipation in the Symposium and Pathology Conference, will be held. Papers of general interest to pathologists will be included on this program. Some of the featured speakers will be Dr. Paul C. Aebersold, Oak Ridge Institute of Nuclear Studies; Dr. J. J. Bittner, University of Minnesota Medical School; Dr. Frank W. Foote, Memorial Hospital, New York City; Dr. W. C. Hueper, National Cancer Institute; Dr. Fred W. Stewart, Memorial Hospital, New York City; Dr. Roger J. Williams, the University of Texas.

Dr. Fred W. Stewart will deliver the second Bertner Foundation Lecture at the Banquet on April 21. All meetings will be held at the Shamrock Hotel, Houston, Texas. Further information may be obtained from William O. Russell, M. D., 2310 Baldwin Street, Houston, Texas.

AWARD OF FELLOWSHIPS

The Board of Directors of the James Picker Foundation has announced the award of two fellowhips and one grant in radiological research, made on recommendation of the Committee on Radiology of the National Research Council, and administered by the Council.

The fellowship awards were made to: Dr. Frederick G. Sherman, Brown University, who will study the effects of ionizing radiations on enzyme activities of micro-organisms at the University of Stockholm under Dr. George Hevesy; and Dr. Halvor Vermund, University of Minnesota, who will study the effects of roentgen irradiation on incorporation of radiophosphorus into intracellular constituents of transplanted mouse mammary carcinoma, at that institution with Drs. K. W. Stenstrom, C. P. Barnum, and R. A. Huseby.

The research grant was made to the Zoophysiological Laboratory, University of Copenhagen, Denmark, to enable Dr.

Hilde Levi to carry out radioautographic studies of alpha- and soft beta-emitters in animal tissue.

BERTNER FOUNDATION LECTURE

The University of Texas M. D. Anderson Hospital for Cancer Research, in the Texas Medical Center at Houston, Texas, wishes to make the following announcement.

The 1951 Bertner Foundation Lecture will be presented by Dr. Fred W. Stewart of Memorial Hospital, New York City. Dr. Stewart will deliver this lecture on April 21, 1951, at the Shamrock Hotel in Houston, on the occasion of the banquet of the Anderson Hospital's Fifth Annual Symposium on Fundamental Cancer Research.

Establishment of the Bertner lectureship was announced at the Fourth Annual Symposium in 1950. Dr. C. P. Rhoads delivered the first Bertner Foundation Lecture at that meeting. The lectureship is awarded each year to a person selected as having made outstanding contributions to cancer research during the year, or for eminent work in some phase of cancer investigation.

NATIONAL BUREAU OF STANDARDS SEMICENTENNIAL

The year 1951 marks the Fiftieth Anniversary of the National Bureau of Standards. A large number of the principal scientific and technical organizations of the Nation, in recognition of the role of the Bureau in science, have planned meetings in Washington in 1951 to honor the Bureau's Semicentennial. The present calendar of major meetings is presented below. Some of the meetings have regularly been held in Washington in the past; most of them were planned for Washington by the societies in view of the Bureau's Semicentennial.

American Society of Photogrammetry, January 10–12.
Joint AIEE-IRE-NBS Conference on High Frequency Measurements, January 10–12.
American Crystallographic Association, February 15–17.
Inter-Society Color Council, February 28.
Optical Society of America, February 28, March 1–3.
Electrochemical Society, April 8–12.
Union Radio Scientifique Internationale, April 16–18.
National Academy of Sciences, April 23–25.
APS Division of High Polymer Physics, April 26–28.
Bone Char Conference II, May 3–4.
Acoustical Society of America, May 10–12.
Horological Institute of America, May 14–15.
Society for Experimental Stress Analysis, May 16–18.
National Conference on Weights and Measures, May 22–25.
Analytical Division of the American Chemical Society, June 14–16.
American Astronomical Society, June 21–23.
Illuminating Engineering Society, August 26–31, September 1.
International Union of Chemistry, September 13–15.
American Roentgen Ray Society, September 25–28.
American Dental Association, October 15–20.
National Institute of Governmental Purchasing, October 21–24.
Institute of Mathematical Statistics, October 26–27.
American Mathematical Society, October 27.
Conference on Electrical Insulation (NRC), October 29–31.
APS Division of Electron Physics, November 1–3.

In addition, a number of committee conferences and meetings of local sections of societies will be held at the National Bureau of Standards. The Bureau is also planning a series of symposia on special topics, to be held during the year.

Created by Act of Congress on March 3, 1901, the Bureau is the principal agency of the Federal Government for fundamental research in physics, mathematics, chemistry, and engineering. The Bureau's activities are thus largely concerned with the physical sciences although the close interrelationships of the major fields of science preclude the drawing of sharp lines of distinction. Considerable work, for example, is undertaken in biochemistry and biophysics, particularly projects relating to

materials, processes, and instrumentation.

The history of the Bureau actually extends back to the Constitution, which gave cognizance of weights and measures to the Federal Government. An Office of Weights and Measures grew out of various acts of Congress beginning in 1830, and this Office was the immediate antecedent of the Bureau.

At the close of the last century, American industry and science recognized the need for a major, national physical laboratory similar to those established in England and Germany. Problems relating to fundamental standards of science, physical constants, properties of materials, and methods and instruments of measurement called for a laboratory that would serve the entire nation. Industry, in particular, had needs for fundamental standards of measurement and ready access to a source of calibration of industrial and laboratory working standards.

All working standards in research laboratories and industry are calibrated in terms of the national standards of physical measurement which the Bureau maintains. In addition, the Bureau carries on necessary research leading to improvements in such standards and in related measurement methods and instruments. New standards, methods, and instruments, in keeping with demands for greater precision and the opening up of new fields of science and industry, are also objects of research.

An equally significant aspect of the Bureau's work is that concerned with specific research and development projects in the physical sciences and mathematics. Some of these projects are related to fundamental standards, properties of materials, and physical constants as well as measurement problems. For example, the development of the atomic clock is directly related to the Bureau's interest in a better standard of time and frequency, and it is also linked to problems in the field of microwave spectroscopy. Others of these projects range in subject matter from pure research in mathematics, in nuclear physics, and in supersonic aerodynamics to the development of guided missiles, proximity fuses, and automatic electronic computing machines.

The scope of the Bureau's work is suggested by the names of its fifteen divisions: electricity, optics and metrology, heat and power, atomic and radiation physics, chemistry, mechanics, organic and fibrous materials, metallurgy, mineral products, building technology, applied mathematics, electronics, ordnance development, radio propagation, and missile development. The divisions in turn consist of several sections—totalling 108—organized as logical units of the divisions. In addition to laboratory work, the Bureau, by virtue of its staff and facilities, is called upon to render scientific advisory services to the Government and industry. Its participation in the activities of scientific and engineering societies and bodies, both nationally and internationally, is necessarily extensive and varied.

OAK RIDGE SUMMER SYMPOSIUM

The Oak Ridge Summer Symposium for 1951 will be in nuclear engineering. The symposia are sponsored annually by the Oak Ridge National Laboratory and the Oak Ridge Institute of Nuclear Studies. They are intended for Oak Ridge personnel, representatives of universities and industrial organizations, and other interested individuals.

The sponsoring organizations decided to devote the symposium to engineering this year following a request to this effect by a a Committee on Nuclear Engineering of the American Society for Engineering Education.

The symposium will be held from August 27 to September 6, 1951. Symposium leaders will include Oak Ridge National Laboratory personnel and invited visitors.

The symposium is expected to cover such subjects as basic nuclear engineering, general nuclear power "philosophy," application of the engineering sciences to nuclear technology, and will emphasize nuclear engineering education.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

Diagnosis and Treatment of Tumors of the Head and Neck. (Not Including the Central Nervous System.) By Grant E. Ward, M.D., D.Sc., F.A.C.S., and James W. Hendrick, M.D., M.S., from the Departments of Surgery of the School of Medicine, University of Maryland, and the Johns Hopkins University School of Medicine, and the Oncology Clinic of the University Hospital and the Tumor Clinic of the Johns Hopkins Hospital. Cloth. Price, $15.00. Pp. 832, with 637 illustrations. The Williams & Wilkins Company, Mount Royal and Guilford Avenues, Baltimore, Maryland, 1950.

This large volume which describes in great detail the tumors that involve the face, neck, lips, mouth, throat, jaws, salivary glands, paranasal sinuses, nose, eyes, ears and skull should be considered a system because the contributions of eleven authors are included. The most valuable portion of the introduction consists of Ward's brief description of the principles of electrosurgery, a method in which he is very experienced. This is followed by an extensive review of the embryology of the head and neck by Vernon E. Krahl. The remainder of the book deals with diagnosis and treatment and no effort has been spared to include photographs and drawings in profusion. The final chapters dealing with the rehabilitation of the face and jaws after deforming surgery are very valuable.

As might be expected in a treatise written by surgeons for surgeons, operative measures are stressed and the techniques and indications given for radiation therapy are often at variance with those used in many irradiation cenetrs. For example, in the section on skin cancer the authors state: "We feel that squamous cell carcinomas over 1.5 to 2 cm in diameter are best treated by surgical measures," and in the section on intraoral cancer they say "Radiation therapy given in sufficient quantities to eradicate squamous cell cancer in the mouth causes permanent tissue damage in the surrounding normal structures resulting in a high percentage of secondary necrosis of the soft parts and bone." Undoubtedly the techniques which they describe do produce such sequelae and their belief that every cancer of the tongue should be resected after irradiation when possible is understandable. Your reviewer cannot refrain from expressing the opinion that some of their techniques such as the heroic procedure consisting of large doses of unfiltered intraoral and filtered external roentgen rays combined with radon seed implantation advocated for cancer of the tonsil may be responsible for the poor standing enjoyed by radiation therapy in many of the large teaching centers of this country.

This book was obviously written as a review of the huge material studied in the tumor clinics of Baltimore and as such it forms a comprehensive atlas of the countless varieties of tumors of the head and neck. Certainly a careful study of the clinical material portrayed will be very helpful to all radiation therapists who treat such lesions.

Charles L. Martin, M.D.

Betekenis en Bepaling van de Skeletleeftijd. With a Summary and an Atlas in English. Avec un résumé et un atlas en français. Door Bernard Speijer, Geboren te 's Gravenhage. Paper. Pp. 153, with 210 illustrations. Eduardo Ijdo N. V., Leiden, Netherlands, 1950.

This is a monograph on the significance and determination of skeletal age of children. The text sumarizes the factors influencing skeletal development, illustrated by roentgenograms of the author's patients. The author has assembled an atlas based on roentgenograms of the hand and pelvis of 360 healthy children, ten boys and ten girls at each year of age from three years to twenty years.

The author brings forward the following opinions on the basis of his study: That skeletal development proceeds in two waves, and that in girls of eight and nine years of age development is very slow, and in boys of ten, eleven, and twelve years development is practically arrested. Skeletal development is resumed in both sexes during the preadolescent period, the growth spurt probably being induced by sex hormones. The variability of the bone age seems

to be ±2 years, except in boys aged ten, eleven, and twelve years, where the variability is ±4 years.

Probably one reason that the author postulates slow development of the skeleton at certain ages is that he relies primarily on onset of ossification and on the time of epiphyseal fusion to assess bone age. Unless he were to use more definite intermediate indicators of progress toward maturity, he might well conclude that there are long intervals in which development is slow.

The reader will probably wish that the reproduction of the roentgenograms could have been better. Also it seems doubtful whether ten children at a given age are enough to determine the average developmental status, and the range of variation in healthy children. If the same children could have been examined over a period of years, the author's conclusions would have had more validity.

However, this monograph will add to our knowledge of skeletal growth in healthy children, and deserves careful study.

Normand L. Hoerr, M.D.

Klinische Pathologie der Blutkrankheiten. Von Prof. Dr. Rudolf Schoen, Direktor der Medizinischen Universitätsklinik zu Göttingen; und Prof. Dr. Walter Tischendorf, Oberarzt der Medizinischen Universitätsklinik zu Göttingen. Cloth. Price, DM 57.–. Pp. 521, with 101 illustrations. Georg Thieme. Diemershaldenstrasse, 47, Stuttgart, Germany, 1950.

The main purpose of this volume, according to the authors, is to correlate the fundamentals of the pathological physiology and pathogenesis of blood diseases with their clinical picture. The fundamentals are comprehensively presented but the clinical discussions are sometimes sketchy and lacking in completeness.

The book is composed of the following chapters: Morphology and Development of Blood Forming Tissues and Blood Cells; Physiology and Pathology of Production and Destruction of Blood Cells; Methods of Blood Examination; Anemias; Myeloid Insufficiencies; Hemorrhagic Disorders; Relation of the Spleen to Blood Disorders; Erythremias, Leukemias, Tumor and Tumor-like Conditions Involving Blood Forming Tissues; Leukemoid Reactions; and Inherited and Familial Blood Diseases.

Ample discussions of the most recent advances in hematology are included. An extensive bibliography follows each chapter, with many references to the American and English literature. The book is illustrated with good photomicrographs and reproductions. Additional colored plates, however, would enhance the value of this volume. Small print on poor paper makes prolonged reading difficult.

The subject material is well organized and helpful marginal notes indicate subdivisions in the text. The appendix includes a subject index of fourteen pages and authors' index.

The book is of value to hematologists and internists particularly with respect to its inclusion of recent developments, but generally it will be of limited usefulness in the English speaking countries.

Stefan S. Fajans, M.D.

Cancer. A Manual for Practitioners. Second edition. Cloth. Price, $2.00. Pp. 308. Published by the American Cancer Society (Massachusetts Division), Inc., 462 Boylston Street, Boston 16, Massachusetts, 1950.

This, the second edition of a manual published initially in 1940, is a cooperative effort of the American Cancer Society (Massachusetts Division), Inc. and the Massachusetts Department of Public Health. It is primarily designed to aid the general practitioner in the diagnosis and management of various types of cancer. It goes beyond this aim, however, and provides a concise presentation of the many complex problems related to present day cancer research, clinical management and education.

Beginning with a brief historical sketch of our knowledge of cancer, chapters are devoted to discussions of trends in cancer research, epidemiology, pathology, diagnosis and irradiation. The treatment of malignant diseases by irradiation is presented in a simplified style outlining its general indications, limitations and hazards. The clinical aspects of neoplasms arising primarily in the various organs and tissues are individually discussed. Although a number of collaborators, outstanding in their special fields, have participated in the preparation of the book, a central plan has been followed whereby the early symptoms, diagnosis and pathology of each neoplasm is stressed. Details of treatment have been wisely omitted but the relative merits of surgery, irradiation, hormone therapy and chemotherapy are discussed.

The value of surgical procedures when feasi-

ble is given proper emphasis throughout. An entire, and extremely valuable, chapter is devoted to a discussion of the measures which may provide relief and comfort to the patient with hopelessly advanced cancer. The established place of hormone therapy in the management of advanced carcinoma of the breast and prostate gland is reviewed. In the final chapters, the activities of various organizations devoted to cancer control are correlated.

This edition contains a wealth of information that should prove valuable to every physician. Its usefulness will not be limited to the general practitioner alone but till provide specialists in all fields a kaleidoscopic view of the progress being made in the control of malignant diseases. It is a laudable venture in cancer education.

MARION S. DEWEESE, M.D.

HANDBOOK OF PHYSICAL MEDICINE AND REHABILITATION. Selections authorized for publication by The Council on Physical Medicine and Rehabilitation, American Medical Association. Published for the American Medical Association. Cloth. Price, $4.25. Pp. 573, with 56 illustrations and 25 tables. The Blakiston Company, 1012 Walnut Street, Philadelphia 5, Pennsylvania, 1950.

The Handbook of Physical Medicine is published for the first time and in a new form by The Blakiston Company. It was originally *The Handbook of Physical Therapy* and later *The Handbook of Physical Medicine* published by the American Medical Association. It is at present still sponsored by the Council on Physical Medicine and Rehabilitation of the American Medical Association. Many of the articles are as they were in the previous edition, and some of them have been rewritten.

The book shows both the advantages and the disadvantages of its past. Some of the authors are by now deceased, and their articles have not been rewritten. Individual contributions are by authorities in the field and carry much of their personal views and contributions.

Unusually valuable articles are the articles on "The Physiologic Effect of Heat" by Wakim, and the following article on "Medical Diathermy" by Martin and Erickson, all from the Mayo Clinic. Considerable work has recently been done, particularly by workers from the Mayo Clinic on the use of Ultra Short Wave Diathermy, the so-called Microtherm. This article is written with considerable restraint, and the authors realize that "clinical use of microwaves is only now beginning. However, careful clinical experience for a period of years, carried out by careful observers, will be required before the clinical status of diathermy with microwaves can be definitely established. Although the apparatus for diathermy with microwaves has been approved by the Council on Physical Medicine and Rehabilitation, definite care and precautions should be taken in its use which should be confined to members of the medical profession."

Of unusual interest also as a modern development is the article by Osborne on "Direct Current Applications and Electrical Stimulation of Muscle," and that by Hallowell Davis on "Application of Physical Medicine to Problems of Hearing."

H. D. BOUMAN, M.D.

LIGHT THERAPY. By Richard Kovacs, M.D., Professor of Physical Medicine, New York Polyclinic Medical School and Hospital. Fabrikoid. Price, $2.25. Pp. 112, with 28 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1950.

Dr. Kovacs is a well known author in the field of light therapy and electrotherapy, and has already published many larger books than the present little volume on the same subject. The present book can be considered as a short résumé of Dr. Kovacs' more intensive writings, and as such should prove to be very valuable to those who are using light therapy without desiring all the information that a specialist in physical medicine might want to have.

H. D. BOUMAN, M.D.

BOOKS RECEIVED

PEDIATRIC X-RAY DIAGNOSIS. A Textbook for Students and Practitioners of Pediatrics, Surgery and Radiology. By John Caffey, A. B., M.D., Professor of Clinical Pediatrics, College of Physicians and Surgeons, Columbia University; Attending Pediatrician and Roentgenologist, Babies Hospital and Vanderbilt Clinic, New York City; etc. Second edition. Cloth. Price, $22.50. Pp. 862, with 1,039 illustrations. Year Book Publishers, Inc., 200 East Illinois Street, Chicago, Illinois, 1950.

THE ESOPHAGUS AND PHARYNX IN ACTION. A Study of Structure in Relation to Function. By William Lerche, M.D., Fellow, American College of Sur-

geons; Founder Member and Honorary Member of the American Association for Thoracic Surgery; Formerly, Associate Professor of Surgery, University of Minnesota, Minneapolis, Minnesota. Cloth. Price, $5.50. Pp. 222, with 93 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois. 1950.

Gastritis, Ulkus und Karzinom. Röntgenstudie unter Berücksichtigung formal-genetischer Beziehungen. Von Prof. Dr. J. Bücker, Chefarzt der Röntgen-abteilung des Allgemeinen Krankenhauses, Heidberg, Hamburg. Paper. Price, $2.75. Pp. 89, with 82 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany, 1950.

Post-Graduate Lectures on Orthopedic Diagnosis and Indications. By Arthur Steindler, M.D., F.A.C.S., Professor of Orthopedic Surgery, State University of Iowa, Iowa City, Iowa. Volume I. Section A: Propedeutics in Orthopedic Diagnosis. Section B: Congenital Deformities and Disabilities. Cloth. Price, $7.50. Pp. 289, with 290 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1950.

The 1950 Year Book of Radiology. (June, 1949–June, 1950.) Radiologic Diagnosis, Edited by Fred Jenner Hodges, M.D., Professor and Chairman, Department of Roentgenology, University of Michigan; and John Floyd Holt, M.D., Associate Professor, Department of Roentgenology, University of Michigan. Radiation Therapy, Edited by Isadore Lampe, M.D., Associate Professor, Department of Roentgenology, University of Michigan; and Robert S. Mac Intyre, M.D., Assistant Professor, Department of Roentgenology, University of Michigan. Cloth. Price, $6.75. Pp. 480, with 400 illustrations. Year Book Publishers, Inc., 200 East Illinois Street, Chicago, Illinois, 1950.

Diagnostic Roentgenology. Volume I. By Ross Golden, M.D., Editor, Professor of Radiology, The College of Physicians and Surgeons, Columbia University; Director of the Department of Radiologic Service, The Presbyterian Hospital, New York. Fourth issue of renewal pages. Thomas Nelson & Sons, 385 Madison Avenue, New York 17, New York, 1950.

Essentials of Urology. By J. C. Ainsworth-Davis, M.A., M.D., B.Ch. (Cant.), F.R.C.S. (Eng. and Edin.), Urological Surgeon, The Bolingbroke Hospital, London; Visiting Urologist, Kettering and District General Hospital and the Lord Mayor Treloar's Hospital, Alton; etc. Cloth. Price, $10.00. Pp. 734, with 512 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1950.

"Your Prostate Gland." Letters from a Surgeon to His Father. By Reed M. Nesbit, M.D., Professor of Surgery, University of Michigan Medical School; Chief, Section on Urology, University Hospital, Ann Arbor, Michigan. Illustrations by Janet McLaughlin. Cloth. Price, $2.00. Pp. 50, with several illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1950.

Radiation Therapy in the Management of Cancer of the Uterine Cervix. By Simeon T. Cantril, M.D., Director, Tumor Institute of the Swedish Hospital, Seattle, Washington. Cloth. Price, $5.00. Pp. 196, with 25 illustrations and 29 tables. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1950.

The Results of Radium and X-Ray Therapy in Malignant Disease. Being the Third Statistical Report from the Radium Institute, The Christie Hospital and Holt Radium Institute, Manchester. Years 1940 to 1944 inclusive assessed at 5 years and 1934 to 1938 assessed at 10 years. Compiled by Ralston Paterson, Margaret Tod and Marion Russell. Cloth. Price, $2.50. Pp. 167, with numerous tables. E. & S. Livingstone Ltd., 16–17 Teviot Place, Edinburgh, Scotland, 1950.

Atlas of Tumor Pathology. Section II—Fascicle 6. Tumors of the Peripheral Nervous System. By Arthur Purdy Stout, M.D., Professor of Surgery, Columbia University, College of Physicians and Surgeons, New York City. Published by the Armed Forces Institute of Pathology. Under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C., 1949. Paper. Price, $.60. Pp. 57, with 56 illustrations. American Registry of Pathology, Armed Forces Institute of Pathology, Washington 25, D.C.

Le nouveau pavillon de Radiologie à l'Hôpital de Bavière. Paper. Pp. 62, with numerous illustrations. Service de Radiologie et Centre Anticancereux de l'Université de Liège, Liège, France, 1950.

Radiologia Austriaca. Herausgegeben von der Österreichischen Röntgen-Gesellschaft. Band III. Cardboard. Pp. 202, with 70 illustrations. Urban & Schwarzenberg, Wien, IX/71, Frankgasse 4 (Schliessfach 4), 1950.

Eyes and Industry. Formerly Industrial Ophthalmology. By Hedwig S. Kuhn, M.D., Industrial Ophthalmologist, Hammond, Indiana. Second edition. Cloth. Price, $8.50. Pp. 378, with 151 illustrations including 3 color plates. C. V. Mosby Company, 3207 Washington Boulevard, St. Louis 3, Missouri, 1950.

Vol. 65, No. 4

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Neck and Chest

Monro, R. S. The natural history of carotid body tumors and their diagnosis and treatment; with a report of five cases. *Brit. J. Surg.*, April, 1950, *37*, 445–453.

The author has added 5 cases to the 225 reported cases of carotid body tumors. These tumors are usually solitary, slow growing, with no predilection for either sex. They show no definite histopathologic criteria indicative of malignancy. Some of the operated cases developed local recurrence, and a few of the reported cases exhibited the presence of hematogenous bone metastases. They vary widely in their gross and histopathologic appearance.

The diagnosis of a carotid body tumor should be entertained when any solitary tumor is found below and adjacent to the angle of the jaw, particularly if there is marked pulsation. The most important point is the exact relationship of the carotid vessels to the tumor. It is usually possible to trace the carotid vessels as they embrace the tumor, the internal posteriorly and the external anteriorly. It is the only tumor in this region in which a vessel can be felt pulsating in front of the tumor.

The treatment is operative. If refused, radiation therapy is advised. Operation should not be performed before the collateral carotid circulation has been investigated, followed by a suitable interval to allow it to develop to its maximum. Whenever possible, the tumor should be removed by simple dissection with preservation of the carotid vessels. If the carotids must be removed, vein grafts of the common and internal carotids should be performed.

The author's cases are reported in detail.—*Norman Heilbrun, M.D.*

Ward, Grant E., Hendrick, J. W., and Chambers, R. G. Carcinoma of the thyroid gland. *Ann. Surg.*, April, 1950, *131*, 473–493.

In an analysis of 112 cases of carcinoma of the thyroid gland there were 22 cases under thirty years of age, 3 of which were under ten. It is one of the more frequent cancers of the neck in children. Eighty per cent of thyroid cancers have their origin in fetal adenoma. Four to 20 per cent of discrete adenomas develop into cancer. Seventy-seven per cent of this series had a history of pre-existing thyroid abnormality. The relationship between hyperthyroidism and cancer is discussed. The authors state that the association of the two is not clear.

Malignant tumors of the thyroid are grouped into 3 classes:

I. Malignant adenomas—Most of these tumors are of Grade 1-2, and Grahams considers blood vessel invasion as a criterion of malignancy. Distant metastases may occur with little change in the parent tumor. Metastases to the regional nodes by the lymphatics does not occur, as a rule, until the growth has invaded or infiltrated the capsule. The impression is given that the so-called lateral aberrant thyroid tissue cancers are metastatic from the adjacent thyroid and that removal of that lobe and a radical neck dissection are required. Cases are presented illustrating this point.

II. Moderate degree of malignancy—This group consists of papillary adenocarcinomas, alveolar adenocarcinomas and Hürthle cell carcinomas of a moderate degree of malignancy. Growth is slow and a hemithyroidectomy with removal of the isthmus and a radical neck dissection result in non-recurrence in a sizable percentage of cases.

III. High degree of malignancy—This group presents a wide variety of histopathologic patterns, with rapid growth and invasion of adjacent tissues. Clinically and histopathologically they may resemble thyroiditis, especially of the Hashimoto variety. Clinically the hardness of the tumor may resemble Riedel's struma.

The criteria of malignancy are discussed. Four types of adenoma are presented. The lymphatic system is depicted and drainage areas from various parts of the gland shown. In this series the average duration of the nodule before consultation was 3.8 years with the range from two weeks to thirty-eight years. Recent increase in size of the gland or nodule, bosselation and areas of hardness, and hoarsenesss are suggestive of cancer. Hemorrhage in an adenoma causes it to be tense and tender whereas malignant change develops firmness, nodularity and fixation.

Treatment is primarily surgical, with radiation therapy a valuable adjunct when the lesion has extended to the contiguous structures of their regional metastases. Radiation therapy is of value in the inoperable cases and local recurrences. Radioactive iodine therapy is discussed.

Prognosis is best in the early cases developing from the discrete adenoma. Throughout the article emphasis is placed on the removal of the premalignant or simple adenoma.—*J. M. Dell, Jr., M.D.*

Brintnall, E. S., and Kridelbaugh, W. W. Congenital diverticulum of the posterior hypopharynx simulating atresia of the esophagus. *Ann. Surg.*, April, 1950, *131*, 564–574.

Two cases of congenital diverticula of the posterior hypopharynx simulating atresia of the esophagus are presented. Both patients had their mediastinal areas explored, with negative findings. One case had a diverticulectomy. Both cases died and were autopsied. At autopsy a diverticulum of the hypopharynx was found. The cases were two and eight days of age. After reviews of the cases the authors could find no clinical or roentgenographic criteria to differentiate these cases from true atresia of the thoracic esophagus. They feel that pharyn-

goscopy should differentiate the two and advocate this on all cases of suspected atresia. The literature is reviewed and these are apparently the only 2 cases in this location reported.—*J. M. Dell, Jr., M.D.*

Dunhill, Thomas. Pharyngeal diverticulum. *Brit. J. Surg.*, April, 1950, *37*, 404–415.

The author discusses his experience with 28 patients with pharyngeal diverticulum—19 males and 9 females. Twenty-one were operated upon. In 1 case the diverticulum was complicated by the presence of carcinoma arising in the pouch. This was the only fatality.

The diverticula as a rule arise in the midline posteriorly at the junction of the oblique and annular (cricopharyngeus) fibers of the inferior constrictor muscle. An occasional one arises laterally in a slit imbedded in fatty tissue below the cricopharyngeus and the upper fibers of the esophagus.

Although the current view of the etiology is that the condition is due to disordered physiology with incomplete relaxation of the cricopharyngeus, the author points out this does not seem altogether satisfactory for the following reasons: (1) Following radical operations the condition is cured without recurrence while the alleged causes still remain. (2) A diverticulum may be present in several members of one family. (3) It may be found during routine roentgen examination without the patient being aware of its presence.

The symptoms are quite typical, consisting of dysphagia, regurgitation, gurgling, spill over in recumbent position, cough, etc.

The diagnosis is made by roentgen examination which gives characteristic findings. If the contour of the pouch is irregular, the presence of a tumor should be suspected. The one-stage operative technique is described in detail.—*Norman Heilbrun, M.D.*

Kinney, Janet. Tuberculosis in B.C.G. vaccinated nurses. *Ann. Int. Med.*, April, 1950, *32*, 673–681.

In the first seven years of B.C.G. vaccination at the Cook County Hospital Nursing School, as reported by Rosenthal (*J.A.M.A.*, 1948, *136*, 73–78), there were 3 cases of pulmonary tuberculosis in 199 controls and 1 case in 142 vaccinated nurses. Since that report there has been 1 additional case in the vaccinated group and three in the control group.

Two cases are presented to illustrate the manifestations of tuberculosis in B.C.G. vaccinated adults. Both cases had their onset two years after vaccination at twenty-seven and twenty-eight months. These nurses were exposed in tuberculosis wards. Both of them had explosive onsets after what was presumably a short incubation period—four and six weeks—after the onset of heavy exposure.

The clinical courses were interesting. The first case ran a hectic temperature with minimum nodal involvement; the second ran a low grade fever with rather extensive parenchymal and nodal involvement. Both these students showed very little general reaction. They ate well, slept well, felt well, and had no complaints other than impatience with bed rest.

In both cases lymph node involvement was predominant. It is interesting that at the end of the second year the first case had no calcification.

These cases do not resemble the reinfection type of tuberculosis which is seen in unvaccinated nurses. They suggest that B.C.G. has modified the course of the tuberculous infection.—*J. J. McCort, M.D.*

Weens, H. Stephen, and Thompson, Edgar A. The pulmonary air meniscus. *Radiology*, May, 1950, *54*, 700–705.

The pulmonary air meniscus is a crescent shaped air shadow which partially surrounds an area of increased density in the lung parenchyma. This shadow has been reported in the foreign literature mainly in association with echinococcus cyst but the authors report 3 cases in which the air meniscus was noted in a lung abscess, bronchogenic cyst and possibly in a bronchiectatic cavity.

The explanation of this air shadow is based on the assumption that when the bronchial drainage of a cavity is interfered with, desquamation products, bacteria and fungi may fill the cavity. With absorption of fluid the intracavitary mass then assumes a shape somewhat like the cavity but leaves a small amount of space occupied by air. This combination of factors probably explains the unusual roentgen findings.

One of the cases reported had inspissated material in a lung abscess while the other proved case was that of a mass of fungus tissue in a bronchogenic cyst.—*C. A. Stevenson, M.D.*

Meade, Richard H., Jr., Head, Jerome R., and Moen, Chester W. The management of chylothorax. *J. Thoracic Surg.*, May, 1950, *19*, 709–723.

The literature is reviewed and 3 cases of chylothorax are reported in detail.

Trauma is the most common cause of chylothorax. It may be such an obvious insult as a bullet wound, stab wound or surgical procedure, but, on the other hand, the etiology may be obscure, as pointed out in the authors' first case. The only possible factor here was a fall down the steps three months prior to the onset of symptoms. Sudden hyperextension of the spine could have ruptured the duct fixed to the surface of the vertebrae by inflammation or by congenital bands. In the other 2 cases there was involvement of the retroperitoneal and posterior mediastinal spaces by lymphosarcoma. A marked drop in the number of the lymphocytes and eosinophils in these cases is of great diagnostic value.

The chyle caused an inflammatory reaction with

great thickening of the pleura, and re-expansion of the lung may be very difficult.

The anatomy of the thoracic duct is discussed.

In the treatment of patients with chylothorax, unless operation is needed for an associated thoracic lesion, ligation of the duct should be used only after the simpler methods of treatment by aspiration of the chyle and by closed drainage have failed. Replacement of protein lost in the chyle should be by high protein diet and intravenous administration of amino acids until further experimental work has been done on the cause of reactions following the intravenous administration of the aspirated chyle.—*F. M. Reis, M.D.*

LAPP, RAYMOND. Le traitement médical des abcès pulmonaires et de leurs complications pleurales; importance d'une thérapeutique locale. (The medical treatment of pulmonary abscesses and of their pleural complications; importance of local treatment.) *Schweiz. med. Wchnschr.*, June 10, 1950, *80*, 604–612.

The great importance of local treatment of pulmonary abscesses is emphasized. This has been rendered possible by bronchial instillation of antibiotics and other therapeutic agents into the cavities after accurate localization of the abscesses by roentgenography, tomography, fluoroscopy and bronchoscopy. At times it has been necessary first to instill lipiodol into the cavities for localization and fluoroscopic guidance of the instilling tube. Several excellent chest roentgenograms are presented.—*J. N. Sarian, M.D.*

CUTHBERT, JAMES. Tuberculous empyema; clinical course and management. *Am. Rev. Tuberc.*, May, 1950, *61*, 662–677.

In a series of 7,206 cases of pulmonary tuberculosis treated in Baguley Sanatorium, 146 cases of tuberculous empyema occurred. The term empyema was used to designate a collection of purulent, not merely turbid, fluid. The etiological factors were as follows: contra-selective artificial pneumothoraces (93 cases); spontaneous pneumothoraces (44 cases); operative removal of diseased lung (2 cases); Pott's disease of thoracic spine (1 case); and 5 out of the remaining 6 probably were associated with spontaneous pneumothorax. In the sixth case there was minimal parenchymal disease and no other complication.

In some instances the purulent fluid followed a long period of non-purulent fluid; in others the onset was very abrupt. Some cases had only tubercle bacilli in the pus; in others there was mixed infection.

In a total of 105 cases of tuberculous empyema (the cases following spontaneous pneumothorax were not included), irrespective of the type of treatment, only 20 patients recovered completely. Seventy-one patients died within five years, and 6 patients had persistent empyema.

The prognosis with conservative therapy is very poor. The prognosis with surgical treatment is best where surgery is instituted early. The most important causes of failure with conservative therapy are failure of the lung to expand with persistence of a pleural space, bronchopleural fistula, and spread of disease. If the lung has not re-expanded within three months, it probably will not, and the degree of pleural thickening will handicap the surgical procedure. Therefore, it is recommended that the period of conservative treatment be given not more than a six to eight weeks' trial. If re-expansion of the lung has not occurred within this time, surgical treatment should be instituted, unless, of course, there are contraindications such as contralateral disease, severe debilitation, etc.—*Lois Cowan Collins, M.D.*

CARSWELL, JAMES, JR. Arteriovenous fistula of the lung, with report of a case. *J. Thoracic Surg.*, May, 1950, *19*, 789–793.

Since 1942, approximately 28 cases of arteriovenous fistula of the lung have been reported in the literature. The most frequently recorded symptoms are cyanosis, polycythemia, clubbing of the fingers and a pulmonary density on roentgen examination. Inconstant findings are an audible murmur over the lesion and expansile pulsation of the mass fluoroscopically. Dyspnea, hemoptysis and the co-existence of hemangiomas elsewhere in the body may appear as prominent symptoms in some cases of arteriovenous fistula.

The author's case, a male aged twenty, complained of transient mild shooting pains in the interscapular region of two years' duration. Slight polycythemia and minimal finger clubbing were present.

Roentgen examination demonstrated a small circumscribed area of increased density in the posterolateral part of the right base. Bronchograms and bronchoscopy gave no further information. Operation revealed a pulsating mass about 4 cm. in diameter immediately beneath the pleura. The thin pleural covering made it possible to observe the blood eddying within the tumor. The lower lobe was removed and the patient's subsequent course was uneventful.

The reproduced roentgenogram of the inflated, injected specimen showing the relationship of the lesion to the pulmonary vessels is of interest.—*W. W. Maver, M.D.*

WISEMAN, JOSEPH R., BROWN, BERNARD T., and GANDIA, ANTONIO G. Asthma complicated by recurrent spontaneous pneumothorax. *J. Allergy*, May, 1950, *21*, 199–207.

This is a case report. The patient, a male, developed asthma at the age of three and suffered the first spontaneous pneumothorax when thirteen years old. During a period of six years there was a total of

nine major attacks, five on the right, three on the left and one into the mediastinum. On one occasion the right and left sides were involved concurrently, and life was preserved only by hasty thoracocentesis.

Roentgenograms demonstrated numerous apical blebs, rupture of which was considered responsible for the attacks. Right thoracotomy confirmed the presence of blebs which were incised and covered by pleura. There was no recurrence for a period of thirty-five days and left thoracotomy was being deferred at the close of the report.

There is a concise discussion in which the usual benignity of spontaneous pneumothorax is pointed out and emphasis placed on the necessity for definitive treatment if the pneumothorax recurs or becomes chronic. It is stated that the procedure of choice in America is the operation performed on this patient.—*G. M. Wyatt, M.D.*

Phillips, Francis J., Basinger, Clair E., and Adams, William E. Bronchiogenic carcinoma. I. A pathologic clinical correlative study of full-size mounts from operated carcinomas. *J. Thoracic Surg.*, May, 1950, *19*, 680–698.

Cross sections of the entire tumor were studied in 40 resected carcinomas of the lung.

The clinical recognition of carcinoma of the lung is often very difficult because the symptoms and physical findings are unreliable. Many cases were found in routine roentgen examinations. The roentgen examination is valuable as a diagnostic aid primarily insofar as the particular tumor is discretely evident in the lung fields, but it is often helpful as a suggestive indication of pulmonary pathology. Bronchoscopy was done in 95 per cent of the cases and was positive in 65 per cent of these. Resectability can be determined with considerable accuracy by this procedure.

Peripheral tumors showed a greater incidence of metastasis and mortality due to late recognition and consequent more heroic surgical treatment. Central tumors presented symptoms earlier and were removed before sufficient time had elapsed to allow metastasis to take place. The potential malignancy of the adenoma is again stressed. Squamous cell carcinomas predominated in this series and were more centrally located. Together with the adenomas they ranked highest in weight loss, cough and sputum production, but pain was rare. The adeno and squamous cell type, a slowly growing carcinoma, were more peripherally located, had the greater mortality, the least number with hemoptysis, the greatest percentage with emaciation and the lowest percentage with pain. Squamous cells were found in all of the cases excluding the adenomas. Squamous cell and adeno cell carcinoma was demonstrated immediately adjacent within the same tumor mass. The highest percentage of metastasis was found in the adeno and squamous cell group. The adenoma group had 2 cases (50 per cent) with metastasis. The size of the tumor appears to have no relation to the incidence of metastasis. In judging the size of the tumor one may be misled by a chronic pneumonitis surrounding the tumor.

The time of diagnosis of the lung tumor appears to be of more prognostic significance than the type of cell found in the tumor or its location in the lung. Lung carcinoma was found to be six times as frequent in males as in females.—*F. M. Reis, M.D.*

Bogardus, George M., Adams, William E., and Phillips, Francis J. Bronchiogenic carcinoma. II. The correlation of pathologic characteristics and clinical manifestation in unresectable and unexplored post-mortem lung tumors. *J. Thoracic Surg.*, May, 1950, *19*, 699–708.

The authors feel that there is some correlation of cell types with the clinical course. The tumors which appear to be less amenable to surgical therapy are largely the poorly differentiated ones and the adenocarcinomas. This impression is derived from the fact that the autopsied and the explored but not resected tumors were composed of 30 undifferentiated tumors, 17 adenocarcinomas, 16 nonkeratinizing squamous, 4 keratinizing squamous, and 5 mixed forms containing more than one cell type. The squamous carcinoma is a slowly growing, locally invasive, and relatively non-metastasizing growth accompanied by infection, necrosis and cavity formation. It is, as a rule, centrally located and offers the most favorable prognosis for complete resection. The peripherally located undifferentiated tumors and adenocarcinomas have a tendency to metastasize widely and the prognosis is poor.

The average duration of symptoms was as follows: adenocarcinoma, eight months; squamous, four months; mixed type, one month (1 case).

Half of the autopsied but not surgically explored patients were undiagnosed prior to death. Four of these had tiny incidental tumors occurring during the course of other diseases. In the remaining cases, the clinical manifestations were caused by the tumor, but were misinterpreted.—*F. M. Reis, M.D.*

Seiler, Hawley H., Clagett, O. Theron, and McDonald, John R. Pulmonary resection for metastatic malignant lesions. *J. Thoracic Surg.*, May, 1950, *19*, 655–679.

The authors present reports of 52 cases in the literature plus 10 cases at the Mayo Clinic in which pulmonary resection was performed for metastatic malignant lesions. In 57 cases the type of primary tumor was mentioned and, of these, 32 per cent were sarcomas and 68 per cent were carcinomas. The time

interval between removal of the primary tumor and the appearance of the metastatic lesion was extremely variable. In several instances the metastatic lesion was discovered prior to the primary growth or simultaneously. The patients with long intervals of time elapsing between the occurrence of the primary and the secondary tumors did no better than the group as a whole. In a very substantial proportion of cases the tumor was found to be invading a major bronchus and positive results on bronchoscopic biopsy could be obtained. This is in contradistinction to the former teaching that bronchial invasion by a metastatic tumor is uncommon.

Lobectomy or segmental resection is probably the procedure of choice when possible. Out of 35 patients reported living, 2 patients survived ten years or longer and an additional 7 survived for periods ranging from three to ten years. The remaining 14 patients had been living and well for periods varying from several months to two years after resection. The most common primary tumors encountered among the surviving group were carcinoma of the colon and rectum, hypernephroma, fibrosarcoma and carcinoma of the ovary.

In some instances in which there was a final fatal outcome, pulmonary resection resulted in such a degree of palliation and prolongation of life as to make the procedure definitely worthwhile.

Surgical excision of solitary metastatic malignant lesions of the lung is indicated in cases in which there is no evidence of further metastatic spread and in which the primary tumor apparently has been completely removed.—*F. M. Reis, M.D.*

Weir, A. B., Jr., Pulmonary adenomatosis; clinical review and report of three cases. *Arch. Int. Med.*, May, 1950, *85*, 806–818.

This article is a review of the clinical, laboratory and roentgenologic aspects of pulmonary adenomatosis with an attempt to build up a clinical picture. The authors believe the condition is neoplastic and not infectious in origin. Grossly there are two forms while microscopically there is only one. The commoner form is that of multiple small nodules throughout the area involved. Less common is a diffuse form that appears as a consolidated segment of lung. The involved alveoli are lined by low columnar or high cuboidal cells in one or many layers. There may be evidence of congestion or inflammation coexisting. Three new cases are added to the 70 appearing in the literature. Only 33 of these had sufficient clinical data to allow evaluation of the symptoms.

The majority of cases reported are over forty years of age. Cough is almost constant with later profuse watery sputum. Dyspnea is prominent. Fever occurs infrequently but loss of weight, cyanosis, clubbing of fingers and weakness may be present. Leukocytosis is not a feature. Aspiration biopsy may help in establishing the diagnosis. Roentgen studies show two general types of shadows—multiple nodular areas or segmental consolidation. Hilar adenopathy is not observed and bilateral lesions are common.

In summary, the occurrence in middle or late life of persistent cough, characteristic sputum, dyspnea with late cyanosis, hemoptysis, anemia, leukocytosis with usually absent fever, and slowly progressive pulmonary densities on the roentgenograms, should be considered as suggestive of pulmonary adenomatosis.—*G. H. Ramsey, M.D.*

Staub, Wilbert, Grayzel, David M., and Rosenblatt, Philip. Mediastinal parathyroid adenoma; report of a case with unusual fatal course. *Arch. Int. Med.*, May, 1950, *85*, 765–776.

An interesting case of a 7 cm. parathyroid tumor shown by roentgen ray to lie in the left anterior mediastinum just beneath the second rib is reported. A complete workup of the case is given with the necropsy findings.

It is pointed out that while parathyroid tumor is not usually considered in the differential diagnosis of mediastinal tumors, a search of the literature shows that 20 per cent of hyperthyroid adenomas occur in the mediastinum, situated, as a rule, in the superior portion. Frequently these tumors are small but they may be large. A discussion of the cause of death is included since the patient reported had a cardioangiogram with diodrast and further had roentgen therapy over the lesion. The nephrotic changes in the enlarged kidneys with tubular calcification and subacute interstitial nephritis are also discussed in relation to the fatal outcome.—*G. H. Ramsey, M.D.*

Childress, William G., and Adie, George C. Plasma cell tumors of the mediastinum and lung; report of two cases. *J. Thoracic Surg.*, May, 1950, *19*, 794–799.

A review of the literature revealed 127 cases of extramedullary plasma cell tumors, with single instances of plasmocytoma of the lung or mediastinum to a total of approximately 132 instances of such tumors reported in the literature.

Differences of opinion have been expressed regarding the nature of these tumors considered by some as carcinoma, by others as granulomatous lesions resulting from chronic inflammation and by still others as benign neoplasms. Tumors are widely distributed; more often found in the upper part of the respiratory tract, in the nose, nasopharynx, mouth and tonsils, other sites being the stomach, intestines, thyroid gland, kidney, ovary, skin, lymph nodes and spermatic cord.

The authors report 2 cases. One was a thirty-seven

year old male with a sharply circumscribed tumor mass in the posterior mediastinum extending out from the upper pole of the left hilus, and measuring 7 cm. in its greatest diameter. Exploration revealed the tumor to be a plasmocytoma and it was removed. Patient has no evidence of recurrence after four and a half years.

The second case was a twenty-one year old white male whose roentgenograms revealed a dense, fairly well circumscribed elliptical mass in the area of the right middle lobe measuring approximately 4 cm. in its greatest diameter. The lesion was removed and, after consultation, diagnosed as a plasma cell granuloma of the lung. Patient had an uneventful recovery with no symptoms after one and a half years.—*R. D. Moreton, M.D.*

Drash, E. C., and Hyer, Harry J. Mesothelial mediastinal cysts; pericardial celomic cysts of Lambert. *J. Thoracic Surg.*, May, 1950, *19*, 755–768.

The authors report 5 cases, bringing the total that have been recorded in the literature from 1925 to 1948 up to 26. Typically these cysts occur in the cardiophrenic angle adjacent to the pericardium, diaphragm and anterior chest wall. They are covered by the mediastinal pleura and are unilocular, thin-walled and contain clear fluid.

On roentgen examination they appear as smoothly rounded, sharply defined areas of uniform density lying against the pericardium, diaphragm and anterior chest wall. They are indistinguishable from other tumors in the mediastinum, such as parasitic cysts, teratomas, dermoids, lipomas, etc.

The history is noncontributory and is the usual one of cough, dyspnea and chest pain. Only 1 patient in this series of 5 presented chest symptoms. One other had severe indigestion and after operation and removal of a large cyst on the left side the indigestion disappeared. The treatment consists of early exploration and removal because an accurate diagnosis cannot be made otherwise.

Two theories of pathogenesis are discussed at length by the authors who recommend that a uniform terminology be adopted. Based upon Kindred's explanation of the origin of these cysts the authors urge that the term "mesothelial mediastinal cyst" be used in future reports of this disease. —*W. W. Maver, M.D.*

Sano, Machteld E., Weiss, Edward, and Gault, Edwin S. Pleural mesothelioma; further evidence of its histogenesis. *J. Thoracic Surg.*, May, 1950, *19*, 783–788.

The authors present a case of pleural mesothelioma to support the concept of the histogenesis of this lesion, i.e., that these tumors represent primary tumors of the lining cells of the mesothelium rather than metastatic lesions.

It is now generally accepted that there are two types of tumors: the diffuse, rapidly spreading type, which has both a fibrosarcomatous appearance and epithelial-like cells, and the localized, fibrosarcomatous, slowly growing tumor without epithelial-like cells.

In rare instances the epithelial-like element may be absent in the first type as in the case that is described.

A fifty-seven year old male, in good condition, fell and sustained an injury to his right thorax with subsequent sharp pains in the right chest and slight cough. Roentgen examination at this time was negative but he continued to have vague pains. About five months later he was admitted to the hospital and the presence of fluid in the right chest was noted. Except for loss of appetite his general condition was excellent. Bronchoscopy revealed compression of the right main bronchus but no mucosal lesions. At exploratory operation, it was found that the pleura and pericardium were completely involved and postmortem examination showed the tumor to be a mesothelioma with none of the epithelial-like elements present. No tumors were found elsewhere. However, tissue culture, in chicken plasma, revealed the potential epithelial-like cell form and placed it in the rapidly spreading, usually inoperable group. Culture in autogenous plasma revealed the mesothelial character of the cells.

A discussion of the factors influencing the form of mesothelial cell is presented.—*W. W. Maver, M.D.*

Samet, P., Schwedel, J. B., and Mednick, H. Electrokymographic studies in aneurysm of the left ventricle. *Am. Heart J.*, May, 1950, *39*, 749–760.

Myocardial infarction and ventricular aneurysm have been studied extensively in recent years by electrokymography, but this is the first published study in which electrokymograms of the intact left ventricular area and the infarcted or aneurysmal area have been recorded simultaneously without resorting to reference points. Previous studies have yielded the following roentgen kymographic criteria for ventricular aneurysm: (1) diminished or absent pulsations in a localized segment of the left ventricle, (2) systolic expansion, partial or total, of the affected region, and (3) marked diastolic splintering, manifested by irregularities of the curve of diastole. Luisada and Fleischner suggest that the disappearance of, or localized reduction in, the amplitude of the wave of the left ventricular contour and secondly, paradoxical pulsation ("dynamic aneurysm") are electrokymographically pathognomonic of ventricular aneurysm.

Three patients with histories of previous myocardial infarction were studied by electrokymography by the authors, and all showed paradoxical pulsation

with systolic expansion and early diastolic collapse in the affected ventricular region. One of the patients showed no definite abnormality of the ventricular pulsation by careful fluoroscopy, even after the area of paradoxical pulsation was demonstrated by the electrokymogram.—*Harold Fulton, M.D.*

KENAWY, M. R. The syndrome of cardiopulmonary schistosomiasis (cor pulmonale). *Am. Heart J.*, May, 1950, *39*, 678–696.

Bilharzic infestation of the lungs by the ova of the intestinal (*Schistosoma mansoni*) or urinary (*Schistosoma hematobium*) schistosomes produces a widespread obliterative arteriolitis of the pulmonary arterioles which gradually leads, after repeated reinfection of the arterioles by ova, to a marked rise in pulmonary arterial pressure, hypertrophy of the right ventricle, and eventually right-sided heart failure. This syndrome is apparently not uncommon in Egyptian adults and clinically may resemble rheumatic or congenital heart disease. The definitive diagnosis of cardiopulmonary schistosomiasis can be made roentgenographically. There may be seen diffuse mottling of the lungs, or in some cases lesions resembling miliary tubercles. The right ventricle is enlarged and there is gross enlargement of the main pulmonary artery and its branches. In contradistinction to the "mitralized" heart of rheumatic fever, the left auricle is usually not detectably enlarged.

Seven examples of cardiopulmonary bilharziasis are presented and the postmortem findings in one case discussed in detail. Typically the patient is a young adult with urinary symptoms or hepatosplenomegaly who develops dyspnea, precordial pain, syncope, or hemoptysis. Cyanosis is not a constant feature.—*Harold Fulton, M.D.*

MACK, I., HARRIS, R., and KATZ, L. N. Acute cor pulmonale in the absence of pulmonary embolism. *Am. Heart J.*, May, 1950, *39*, 664–677.

Any mechanism leading to sudden marked increase in resistance against which the right ventricle must work will produce acute cor pulmonale, a condition usually thought to be exclusively due to massive pulmonary embolism. Among the various causes are: (1) multiple small emboli in pulmonary arterioles, usually repeated episodes (blood clots from venous circulation, right auricle, right ventricle; amniotic fluid emboli; direct tumor emboli; fat emboli); (2) endolymphatic carcinomatosis of the lung; (3) massive destructive pulmonary disease complicated by any sudden further obliteration of the pulmonary vascular bed, as by extirpative or collapse surgery, spontaneous pneumothorax, massive atelectasis, or extensive pneumonitis; (4) obstruction of main pulmonary artery trunk or its major branches by embolus, thrombus or external pressure (e.g., tumor); (5) sudden development of left-to-right shunt as in rupture of an aortic aneurysm into the pulmonary artery, the right ventricle or the right auricle; or by rupture of the interventricular septum following infarction or ulcerative endocarditis.

Many of these pathologic states can be detected by roentgenography—*i.e.*, the pulmonary changes in association with right ventricular enlargement. It is emphasized, however, that pulmonary arterial hypertension may exist without roentgenologically demonstrable right ventricular enlargement. In this latter group cardiac catheterization will prove of value in detecting the abnormal pulmonary vascular dynamics and in preventing operation or other trauma which would lead to the acute phase of cor pulmonale.—*Harold Fulton, M.D.*

KISNER, WENDELL H., and REGANIS, JOHN C. Pericardial celomic cyst, with symptoms; case report. *J. Thoracic Surg.*, May, 1950, *19*, 779–782.

This is a case report of a pericardial celomic cyst in a male, aged fifty-six, an uncommon lesion, presenting symptoms of discomfort and an uncomfortable feeling in the left chest difficult to describe. No cough, hemoptysis or weight loss was present.

Roentgen examination revealed a well circumscribed mass in the left costophrenic angle anteriorly, approximately 8 cm. in diameter. The possibility of a hernia through the space of Morgagni was excluded by further roentgen study. Two months later, at operation, a thin-walled multilocular cyst about 8 cm. in size was dissected from the pericardium and the diaphragm.

A follow-up examination two months after operation revealed the patient to be in excellent health and free from precordial discomfort. A discussion of the pathology, symptoms, diagnosis and treatment of this lesion supplement the case report. The presence of symptoms attributed to the cyst in this particular case is unusual.—*W. W. Maver, M.D.*

MEREDITH, H. CLARKSON, JR., Tularemic pericarditis: a report of two cases including one of constrictive pericarditis. *Ann. Int. Med.*, April, 1950, *32*, 688–699.

In this paper 2 cases occurring at the University of Virginia Hospital are discussed and all the previously published cases are reviewed.

Case 1 of this report is the first case of tularemic pericarditis treated with streptomycin to be reported. In spite of its apparently beneficial effect streptomycin did not prevent the development of constrictive pericarditis. However, the treatment was not started until late in the fourth month of illness. Surgical removal of the constricting pericardium completely relieved the incapacitating symptoms. The second case is interesting in that at the time of the first admission constrictive peri-

carditis was considered highly probable, but no evidence of this could be found seven years later.—*J. J. McCort, M.D.*

Way, Geoffrey L., and James, G. C. W. General anaesthesia for bronchography in children. *Lancet*, June 10, 1950, *1*, 1073.

The authors were not satisfied with the various methods of general anesthesia and the technique of iodized oil instillation for reasons such as (1) the mixture used was explosive, (2) no airtight closed circuit could be guaranteed, (3) the endotrachela tube was partially blocked by the introduction of the catheter, etc., and they have developed a new method. They have had a special endotracheal tube constructed with a side tube for the introduction of the radiopaque fluid. They employ this with Cobb's endotracheal tube junction which allows suction to be carried out in an emergency. They use an ordinary Boyle's machine without an ether bottle.

Technique. Anesthesia is induced with 5 per cent intravenous sodium thiopentone given slowly (0.5–1.0 g. given to children aged 4 to 12 years). Direct laryngoscopy is performed and the larynx is sprayed with a few minims of 5 per cent cocaine. The special endotracheal tube is lubricated with nupercaine and introduced into the trachea as far as the entry of the side tube. The endotracheal tube is connected to the Cobb's junction of the Boyle's machine (half-open). The gases flowing through the Boyle's machine are nitrous oxide and oxygen in equal volumes passing over trichlorethylene (contained in the chloroform bottle). The radiopaque fluid is injected down the side tube with the patient postured for filling of the bronchial system. The risk of explosion is eliminated, the airway is unobstructed by catheter, and the respirations are quiet and slow, thus giving adequate time for roentgen exposures during the desired phase of respiration. The bronchial tree can be sucked dry and 100 per cent oxygen given with ease and without danger.—*R. K. Arbuckle M.D.*

Moreau, Marcelo H. Contribución a la técnica de la broncografía. (Contribution to the technique of bronchography.) *Prensa méd. argent.*, June 9, 1950, *37*, 1258–1263.

The author presents a review of the various techniques of bronchography as they have developed since Chevalier Jackson in 1907 for the first time insufflated an opaque powder into the bronchial tree with the aid of the bronchoscope. He enumerates seven methods for the introduction of the opaque medium and nine positionings for roentgenography of the different segments of the bronchial tree.

To simplify the matter, he recommends a standardized technique which he describes in detail. This technique requires a table which can be tilted to 60° from the horizontal and a roentgen tube which can be centered in both the vertical and horizontal planes. For roentgenography in the frontal view the cassette is preferably placed against the back of the patient and the normal ray of the horizontal tube is directed to the center of the hemithorax to be explored. In the lateral view the cassette is placed underneath the affected side and the normal ray of the vertical tube is directed perpendicular to the cassette.

The procedure is as follows: (1) the patient is examined on a fasting stomach of at least four hours' duration; (2) a morphine and camphor oil injection is given one-half hour before the examination; (3) spray anesthesia with 2 per cent pantocain is applied to the nasopharynx and larynx; (4) a Nélaton catheter No. 15 or 16 (more recently reinforced with a flexible guide which is drawn before the injection) is introduced through the nose down into the larynx, usually under vocal and more rarely under fluoroscopic control; (5) after fastening the catheter with adhesive tape to the nose and forehead, the patient is placed on the tilt table in the optimal position with an inclination of 10°, 30° and 60° respectively for the upper, middle and lower parts of the bronchial tree; (6) 2 cc. of 1 per cent pantocain is slowly injected through the catheter while warning the patient not to cough; (7) after putting the cassette in place and centering the tube, 10–15 cc. of a 50 per cent iodized oil solution is injected with a 20 cc. syringe and the patient is again warned not to cough; (8) the necessary roentgenograms are taken in the frontal and lateral views, being careful not to move the patient; then an additional 10 cc. of the opaque medium is injected and further roentgenograms are made immediately after the injection and two or three minutes later; if, after developing the films, the findings prove doubtful, still another 5 cc. of the oil is injected and a final set of films is made.

In concluding, the author states that the procedure is very simple, does not require special equipment and can be carried out with reduced technical personnel. Moreover, it can be used advantageously for the intrabronchial administration of medicinal preparations.—*T. Leucutia, M.D.*

Abdomen

Burnett, W. E., Rosemond, G. P., and Bucher, R. M. Mesenteric cysts; report of three cases, in one of which a calcified cyst was present. *Arch. Surg.*, April, 1950, *60*, 699–706.

Mesenteric cysts are among the rarest of all abdominal tumors. The most common site is in the mesentery of the small bowel. Classical signs are those of a low grade intestinal obstruction plus the presence of a mass, usually freely movable. Roentgenograms may aid in the diagnosis, especially

when there is calcification of the walls of the cyst. Since the diagnosis cannot be made positively without an operation, exploration is necessary to rule out other more serious tumors. The treatment consists of enucleation or resection. Three of the author's cases are presented in detail.—*H. R. Fishback, Jr., M.D.*

Bralow, S. P., Spellberg, M., Kroll, H., and Necheles, H. Peptic ulcer in man. Part 3. Evaluation of ulcer therapy. *Am. J. Digest. Dis.*, April, 1950, *17*, 119–124.

In this article the authors have compiled a complete review of all the reports of recurrence rates with medical therapy in peptic ulcer in man published between 1890 and 1948. These results are then summarized into four groups: (1) duodenal, (2) gastric, (3) combined duodenal and gastric, and (4) studies in which neither the type of ulcer nor the number of patients was stated. Most of these reports show that 50 to 79 per cent of eventual recurrences are within the first year.

It is concluded that no definite objective criteria can be established to determine recurrence of ulcer activity. In their series to be published later in an attempt to evaluate properly a new antacid (carmethose Ciba) a recurrence was diagnosed when rehospitalization was necessary for perforation, hemorrhage, obstruction or intractable pain. The mere presence of epigastric distress which could be relieved by antacid or strict diet was not considered a recurrence.—*A. E. Childe, M.D.*

Zimmer, E. A. Klinik und Röntgenologie des Prolapses von Magenschleimhaut in den Pylorus und in den Bulbus duodeni. (Clinical and roentgenological features of prolapse of the gastric mucosa into the pylorus and into the duodenal bulb.) *Schweiz. med. Wchnschr.*, April 8, 1950, *80*, 351–358.

In spite of the fact that the clinical and roentgenological appearances of this disease entity are so striking, it has received little notice until recently, and particularly in the American literature. Most of the well known textbooks of internal medicine describe it insufficiently or not at all. It is probable that most of the cases previously were interpreted as other conditions, as it is sometimes evident only when searched for. Except for peptic ulcer and gastritis, it is the most important of the benign conditions affecting the distal end of the stomach and the duodenal bulb.

Gastric mucosal prolapse may be either unilateral or circular and complete. In the first type, a portion of the prepyloric gastric mucosa slips into or through the pyloric canal, presenting itself on one side of the base of the duodenal bulb, projecting into the lumen. The pyloric sphincter contracts on this mass, the end of which becomes swollen and engorged, while the portion in the canal is stretched out. The second type arises with a complete separation of the prepyloric mucosa from its muscularis. This mucosa slides through the pylorus in the form of a cylinder, propelled by peristalsis, and may remain fixed there in a manner similar to a small intestinal intussusception. This cylinder of tissue presents in the base of the bulb, and a central depression marks the pyloric canal.

Macroscopic examination of a resected specimen often shows the abnormally loose connective tissue in the prepyloric region. Microscopically the usual finding is a chronic gastritis. In most cases the complete picture is shown only by roentgen examination.

According to its extent, prolapse has been classed into three groups. Group I is relatively frequent. A single fold of musoca passes down into the pyloric canal, and peristalsis may even apparently obliterate this fold (Fig. 1, *B*). The normal bulb is shown in Figure 1, *A*.

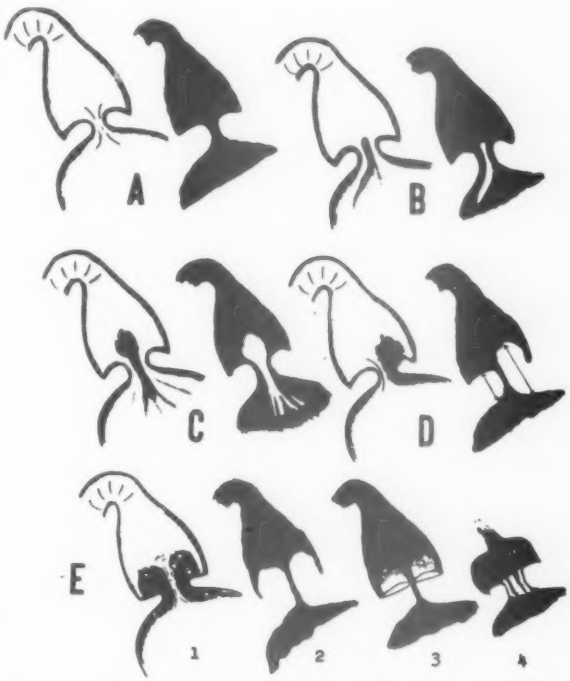


Fig. 1. Diagrammatic representation of the morphologic (white) and roentgen appearance (black) of the prolapse of the gastric mucosa into the pylorus and into the duodenal bulb. (*A*) normal; (*B*) Group I; (*C*) Group II, posteroanterior view; (*D*) Group II, profile view (arrows indicating distances between antrum and bulb); (*E*) Group III, (1) morphologic appearance, (2) ordinary roentgen appearance, (3) "umbrella" appearance, and (4) appearance after emptying of the bulb. (Reproduced by permission from *Schweiz. med. Wchnschr.*, April 8, 1950, *80*, 351–358.)

Group II is made up of cases of unilateral prolapse. A somewhat more voluminous fold slips through the pyloric canal with a bulbous end projecting into the base of the duodenal bulb. This resembles a mushroom, with the head in the duodenal bulb and the stalk in the pyloric canal (Fig. 1, *C* and *D*). It may be noted that on one side the duodenal bulb fornix is more acute, and on that side the pyloric canal is elongated.

Total circular prolapse occurs in Group III (Fig. 1, *E*). The pyloric impression on the base of the bulb is accentuated, and the canal is thereby apparently elongated. The canal may be either narrow or broad. Frequently the apex of the bulb contracts on the mass, permitting only a small amount of barium to fill the bulb.

All stages between Groups I and III occur. Some of these cases have no doubt been diagnosed as polyps in the stomach or bulb, from the similar mushroom appearance. Such pedunculated polyps do occur. In all three groups of prolapse there is antral gastritis with associated spasm, but there is no disturbance in peristalsis otherwise.

It should be determined by fluoroscopy whether or not the prolapse is reducible. When the mass is reducible, at times the pyloric canal and the base of the bulb appear normal. The deformity can usually be brought out with thick barium during active peristalsis. When the prolapse is irreducible, the bulb is never completely filled, and the stomach empties slowly.

The salient roentgen characteristics might be listed as: (1) a filling defect beginning in the antrum and passing into the canal and frequently into the base of the bulb; (2) this may be unilateral or circular, reducible or fixed; (3) absence of disturbance of peristalsis; (4) apparent stenosis of the antrum with possibly a six hour gastric residue; (5) antral gastritis, which is always seen microscopically, sometimes roentgenographically; (6) occasional pain or pressure localized to the pylorus; and (7) hyperperistalsis or occasionally pylorospasm.

This condition is to be differentiated from several other similar abnormalities. In duodenal ulcer the crater is usually on the wall rather than at the base, and it may be associated with radiating folds. A more difficult differentiation is found when, in a scarred ulcer, piling up of mucosa results in the classical signs of prolapse. A few of the features of prolapse are produced by peptic ulcer or other inflammatory lesions near the pylorus, pyloric sphincter hypertrophy, gastric or duodenal polyps, or food residue.

The patient's complaints may be uncharacteristic or may resemble those of peptic ulcer. Frequently there is a feeling of fullness, nausea, pyrosis, vomiting, or intermittent epigastric cramping. With obstruction, the pain may be severe. Secondary anemia is very important if it develops because of bleeding. High gastric acidity is usual, and it must be remembered that peptic ulcer and prolapse may coexist. Prolapse has been seen in patients between the ages of sixteen and seventy without regard to sex.

Mild cases should be treated conservatively with diet, antacids, and antispasmodics. Surgery is resorted to for intractable pain, obstruction, or large or multiple hemorrhages. At operation it may be possible to demonstrate the lesion, if it is not reducible, or show the deformity, if it is reducible, before opening the stomach. Even if it cannot be demonstrated, if there is a clear cut roentgen picture, and if there is no other evident abnormality, the treatment must be that for mucosal prolapse.

The basis for the development of the deformity has not been clearly shown. Some believe that chronic irritation and hypertrophic gastritis are followed by prolapse through hyperperistalsis. Others think that the gastritis is a result of chronic irritation of a segment that was abnormally loose and which prolapsed. It develops only in the presence of several factors, one of which is peristalsis. Because of this fact, the situation of the loose mucosa may vary from time to time, and consequently roentgenologic examination is a much more satisfactory and reliable method than examination at the operating table or study of a resected specimen.—*E. F. Lang, M.D.*

Orie, N. G. M., Van Ridssel, Th. G., and Van der Zwaag, G. L. Pyloric stenosis in sarcoidosis. *Acta med. Scandinav.*, 1950, *138*, 139–143.

An interesting report is given of a woman, aged fifty-three, who had been observed for years because of a diffuse patchy appearance of the lung on roentgen examination. For one year she had complained of nausea and vomiting after meals. Tuberculosis studies were negative. There was only a slight tenderness on applying pressure in the left upper abdominal quadrant. Hypochromic anemia was found. Occult blood and increased fat were found in the stool. Histamine achylia was present. Roentgen study revealed a constant narrowing of the pyloric antrum. On gastroscopic examination the mucous membrane seemed glassy and thickened, the pyloric antrum was rigid, no contraction waves could be observed, and the opening to the duodenal bulb could be seen as a small patent hole.

Gastric resection resulted in a histopathologic diagnosis of sarcoidosis of the prepyloric region of the stomach with involvement of the lymph nodes along the lesser curvature.—*Charles Nice, M.D.*

Smithers, D. Waldron. The association of cancer of the gastric cardia with partial thoracic stomach, short oesophagus and peptic ulceration. *Brit. J. Radiol.*, May, 1950, *23*, 261–269.

It has been suggested that both congenital short esophagus and acquired shortening are actually

sliding hiatal hernias and are due to contraction of the longitudinal muscles of the esophageal wall. This theory has been substantiated by experimental work showing that vagal irritation can produce contraction of the longitudinal esophageal muscles. Various upper abdominal lesions such as peptic ulcers of the stomach and duodenum, cholecystitis, and esophagitis have been mentioned as frequently associated with short esophagus. There must be hiatal insufficiency to permit this shortening to occur.

Only a few cases of cancer of the cardiac end of the stomach in a hiatal hernia have been reported but the author feels that this is misleading. He reports an additional 4 cases, and mentions 2 more. There are three possible explanations for this association. The occurrence may be fortuitous. It may be that the sequence of events, lax hiatus, contraction of the esophagus, hiatal hernia, reflex flow of gastric juice, which leads to esophagitis and peptic ulceration, predisposes to the development of cancer. There is considerable though disconnected evidence that esophagitis does predispose to the development of cancer. The third possibility is that cancer of the cardia is one of the upper abdominal lesions which may lead to shortening so that these tumors may become intrathoracic in a patient with a lax hiatus.—*E. F. Lang, M.D.*

Bjerkelund, C. J., and Husebye, O. W. The clinical and roentgenological findings in steatorrhea of varying etiology. *Am. J. Digest. Dis.*, May, 1950, *17*, 139–149.

The authors studied 12 cases of non-tropical steatorrhea in adults, of which 2 were classified as pancreatogenic, 4 symptomatic, and 6 idiopathic. Serial studies of a standard barium meal were carried out in each case and comparisons made. The cases of idiopathic steatorrhea showed one or more of the usual findings of: (1) dystonia, i.e., variable calibre of the lumen; (2) loss of variability in the mucosal pattern, a sign of decreased autoplasticity, until eventually only circular folds are seen; (3) the moulage sign of sausage-like masses of barium in the intestine, and flocculation of the opaque meal. The cases of pancreatogenic steatorrhea showed only relaxed jejunal loops and no moulage sign. The cases of symptomatic steatorrhea showed changes similar to those in the idiopathic type type except that in 3 of the 4 cases there were findings of localized disease, i.e., reticulosarcoma, Hodgkin's disease and regional jejunitis.

The authors conclude that every case of supposed idiopathic steatorrhea should be examined roentgenologically for organic lesions. Because of the paucity of roentgen changes in the pancreatogenic cases, they suggest that the increased intestinal fat content may not alone be responsible for the roentgen findings in the other cases.—*G. M. Wyatt, M.D.*

Costin, Maurice E., and Gaston, Eugene A. Solitary diverticulum of the cecum. *Arch. Surg.*, April, 1950, *60*, 743–748.

Solitary diverticulum of the cecum represents an acquired type of diverticulum and is a relatively rare condition. The author reports 2 such cases which brings the total number recorded in the literature to only 101. Various explanations are given for the etiology, none of which is considered satisfactory. Differential diagnosis must include appendicitis, carcinoma of the cecum, tuberculosis, actinomycosis, and nonspecific ulcers of the cecum which may perforate.—*H. R. Fishback, Jr., M.D*

Gerwig, Walter H., Jr. Volvulus of the colon. *Arch. Surg.*, April, 1950, *60*, 721–742.

Volvulus of the colon occurs ten times more frequently in Europe than in the United States. As a possible explanation of the difference, diet seems to be one of the most important etiologic factors. Involvement of the sigmoid occurs twice as often as that of the cecum. Diagnostic roentgen study may show the colon proximal to the obstruction to be distended although the small bowel as a rule is deflated. Barium enema will help to locate the obstructed area but the barium may give an "ace of spades" appearance at the site of obstruction. Eight cases of volvulus of the colon are presented in detail by the author.—*H. R. Fishback, Jr., M.D.*

Cantor, Meyer O. Effect of variations in the amount of mercury on the speed of intestinal intubation. *Arch. Surg.*, April, 1950, *60*, 762–770.

This study is the result of intubations in 441 patients utilizing decompression tubes having mercury in their tips. The author feels, that intubation may be speeded up considerably by varying the amount of mercury depending on the patient's condition. He divides the cases as follows: (a) 4–5 cc. of mercury is the optimum amount to be used in the balloon if the patient had no impairment of intestinal tonus or peristaltic activity; (b) in apprehensive and nervous patients, 8–9 cc. of mercury in the tube balloon will facilitate intubation; (c) with atonic or paralytic ileus, 8–9 cc. of mercury produce more successful intubations than 4–5 cc; (d) 2 cc. of mercury in the head of the tube produced successful intubations in 2 patients with atony of the bowel in whom ambulation or change in position could be carried out.—*S. H. Fisher, M.D.*

Palmer, W. L., Kirsner, J. B., and Marshall, H. Therapeutic considerations in chronic ulcerative colitis. *Ann. Int. Med.*, April, 1950, *32*, 627–639.

The treatment of ulcerative colitis is considered by the authors to be an individual problem because

of the great variations in the extent of the disease, its severity, and in its spontaneous course as well as in the personalities of the individuals afflicted. An attempt is made to sketch the varying roles of rest, diet, medication and nursing care, together with the medical, surgical and psychiatric indications. Ulcerative colitis is considered an inflammatory process. Chemotherapy is important even though it is not possible at present to ascribe the disease to any specific organism or to produce complete sterilization of the intestine with the drugs available. Emotional factors are of great importance; they should be recognized and managed by the physician in charge or a psychiatrist. Surgery is indicated primarily for the complications.—*J. J. McCort, M.D.*

Sherwin, Benjamin, and Gordimer, Harry. Aneurysm of the splenic artery; report of two cases. *Ann. Surg.*, April, 1950, *131*, 599–603.

Two cases of aneurysm of the splenic artery are reported, one with successful operation before rupture, one with death after rupture without operation. The literature is reviewed and 15 cases of rupture complicating pregnancy with 14 deaths collected by Cosgrove, Watts and Kaump are recorded. In most cases diagnosis is not made before autopsy or operation, and not in a single one of the cases complicating pregnancy. Many are asymptomatic until rupture. Complaints vary from mild epigastric to severe abdominal pain. In most cases there is some enlargement of the spleen with infarction. Roentgen studies of the abdomen may show a calcified shadow in the left upper abdomen with a sharply delineated periphery and a mottled central portion. In some, a bruit may be heard and a pulsation felt. Treatment is splenectomy with removal of aneurysm. If this is not feasible, ligation of the splenic artery may be used with atrophy of the spleen usually following, but no ill effects. Tamponade is ineffectual.—*J. M. Dell, Jr., M.D.*

Peake, John D., and Eskeridge, Marshall. Hepatic amebiasis with complications. *South. M. J.*, April, 1950, *43*, 300–307.

The chief purpose of this paper is to emphasize the frequency and importance of liver complications in patients infected with *Endamoeba histolytica*. The importance of roentgenologic examination as a diagnostic procedure is stressed. This should consist of careful fluoroscopy and adequate films. It is stated that a correct diagnosis can be made in from 80 to 90 per cent of the cases. The authors quote Ochsner and DeBakey who, in a series of 50 cases of amebic liver abscess, were able to make a positive diagnosis in 87.7 per cent by roentgen examination.

The roentgen findings are: elevation of the right diaphragm; occasional elevation of the left diaphragm, if there is an abscess in the left lobe; fixation of the right diaphragm, particularly if the abscess is near the dome; obliteration of the cardiophrenic angle; and right basal chest involvement, usually consisting of patchy pneumonitis, atelectasis or fluid. There may be bulging of the diaphram if the abscess is pointed.

It is suggested that the stomach and duodenum be filled with barium; if an abscess is present the cap and cardia are displaced and the lesser curvature assumes the typical crescent shape. Aspiration of an abscess cavity and replacement with air followed by roentgenographic studies has been advocated.—*J. G. Snead, M.D.*

Gynecology and Obstetrics

Kaufman, William, and Fiege, Herbert R., Jr. Cytologic diagnosis of malignant disease in a general office practice. *Surg., Gynec. & Obst.*, April, 1950, *90*, 451–454.

This report is based primarily on the examination of smears from the vaginal vault. Most of the smears were obtained from patients entering the practicing physician's office for a general physical examination. For fixation of smears the method recommended by Papanicolaou was used. The smears were then sent to the authors' laboratory and stained according to Papanicolaou's method. Scarcely any clinical information was available to the examiners. The report thus represents a survey made on patients in a general office practice who, in the majority of instances, were not primarily suspected of having cancer.

In the period of January 1, 1948, to May 9, 1949, a total of 1,721 cases came to the authors' attention. The number of smears examined was between 1,900 and 2,000. The results obtained in the survey would serve to indicate that, once experience has been gained, accuracy in diagnosis becomes fairly dependable. While little harm may be done in reporting a smear positive even if biopsy or curettage fails to show any evidence of cancer, a negative report on a smear coming from a patient suffering from malignant disease would be a definite fallacy. Thus, in the report to the physicians, attention was drawn to the fact that a negative report did not exclude cancer and that history, clinical findings and other means of diagnosis should be done to exclude such a possibility. In this series of 1,721 patients entering a doctor's office and in most instances seeking consultation, not because of an indication of cancer but for a general checkup, 47 were considered suspicious and 28 actually found to be suffering from malignant disease. These findings would seem not only to warrant the continuation of such a service to the physician and to the patient but to make it mandatory for the pathologist to familiarize himself thoroughly with this method of diagnosis.—*Mary Frances Vastine, M.D.*

Boldero, J. L., and Kemp, F. H. The diagnosis of hydrops foetalis. *Brit. J. Radiol.*, April, 1950, *23*, 219–224.

The generally accepted diagnostic criterion of hydrops is the "Buddha" position. The essentials of this are: (1) the legs are extended at the hip and flexed at the knee; (2) the arms are directed out laterally from the fetal body; (3) the fetus is in a general state of extension; (4) the lower ribs are splayed; (5) the soft tissue outline of the distended abdomen may at times be seen.

These are the characteristics of advanced hydrops, and at times in the earlier stages they are not present. The authors feel that the diagnosis can be made earlier if the following are present: (1) straightening of the normal fetal kyphosis with extension of the neck; (2) roentgenographic evidence of hydramnios; (3) iso-immunization of the mother.

The characteristic position of the fetus is not due to the presence of hydramnois, but is adaptation to the fetal abdominal soft tissue edema and ascites and the edema of the soft tissues of the neck. It must be remembered that an intra-abdominal tumor of hepatic or renal origin, or the presence of a second fetus, could both cause similar extension of the fetus. Also, the position of the fetus must be seen in a lateral view, or a close approximation to it.—*E. F. Lang, M.D.*

Samuel, Eric, and Cohen, Joel. The prenatal radiological diagnosis of hydrops foetalis. *Brit. J. Radiol.*, April, 1950, *23*, 225–230.

Erythroblastosis fetalis occurs as a result of incompatibility of maternal and fetal blood, and occurs as three clinical types or degrees. Congenital anemia is the mildest type, marked only by anemia. Icterus gravis neonatorum in the more severe cases progresses fatally. The third type, hydrops fetalis, is most severe, and usually results in a stillborn infant. It is marked by generalized edema, ascites, and anemia. Extramedullary erythropoiesis combined with edema produces enlargement of the liver and spleen.

The roentgen changes which are produced vary with the severity of the disease. The "halo sign" has been described as due to edema of the scalp, but the importance of this ring of decreased density has been questioned. A second, more important feature is straightening of the fetal spine, which develops because of enlargement of the liver and spleen, ascites, and anasarca. The same factors produce extension of the thighs at the hips with flexion of the knees. This, with the absence of spinal flexion, has been referred to as the "Buddha" position. This abnormal position can also be produced by other factors.

Osteopetrosis has been described in erythroblastosis fetalis. The authors have demonstrated that, in addition to true osteopetrosis, there is a second factor causing increase in density of the bones in roentgenograms. The edema of the soft tissues produces apparent or pseudo-osteopetrosis.

A case is presented in which the changes described were shown. In addition, enlargement of the placenta is sometimes seen, and was sought for unsuccessfully. The case was interesting because serological tests on the mother had led the clinicians to suspect only mild erythroblastosis, while the roentgen signs correctly showed an advanced stage of the disease.—*E. F. Lang, M.D.*

Macafee, C. H. G. Hydramnios. *J. Obst. & Gynaec. Brit. Emp.*, April, 1950, *57*, 171–182.

The incidence of hydramnios in approximately 12,000 cases was determined to be 1.25 per cent.

In the acute form, the rapid increase in size of the uterus takes place in the early weeks. In the subacute or chronic forms, it is most difficult to diagnose any is rarely noted before the thirtieth week. Difficulty in diagnosis arises mainly when the condition is associated with multiple pregnancy. A roentgenographic examination is essential as a guide to prognosis and treatment. Based on the roentgen findings, the cases are divided into four groups.

a. Gross fetal abnormality either in a single fetus or in one fetus of a multiple pregnancy: 54 cases (57 babies, with only 3 babies surviving), of which 47 had anencephaly and 7 other gross abnormalities. The fetal mortality was 94.6 per cent.

b. No roentgenologically demonstrable abnormality: 78 cases (100 babies with 67 babies surviving, in 20 abnormal babies the widely varying abnormalities being discovered subsequent to delivery). The fetal mortality was 33 per cent.

c. Hydramnios associated with diabetes: 6 cases (3 babies dead, 2 of which were anencephalic, but not included in group a).

d. Hydramnios associated with intrauterine death: 9 cases (Rh incompatibility 3, doubtful cause of death 6).

Summary: Hydramnios during pregnancy appears to be a more serious complication than has perhaps been appreciated. Roentgen diagnosis of abnormal fetus can often be made, but even in the presence of roentgen evidence of a normal baby 33 per cent of the babies are born dead and present unexpected malformations.—*R. K. Arbuckle, M.D.*

Wright, H. P., Osborn, S. B., and Edmonds, D. G. Changes in the rate of flow of venous blood in the leg during pregnancy, measured with radioactive sodium. *Surg., Gynec. & Obst.*, April, 1950, *90*, 481–485.

In a previous publication the authors showed that the average venous blood flow rate was markedly decreased while labor was in progress but that a

normal flow rate had been regained by the fourth to tenth day of the puerperium. They suggested that this was due to mechanical pressure on the large veins as they traverse the pelvis to form the inferior vena cava posteriorly. So striking was the slowing observed in the women during labor that it seemed advisable to determine whether this change occurred only with the commencement of labor or whether it took place gradually as a result of the increase in abdominal pressure produced by ascent of the gravid uterus.

Method. A small volume of radioactive sodium in sodium chloride solution containing 2 to 10 microcuries per milliliter was injected under standard conditions of posture, rest, and temperature, into one of the dorsal veins of the foot and its passage through the femoral vein at the groin recorded by a Geiger-Müller counter. The impulses from the Geiger-Müller counter were relayed in such a way that a permanent kymographic tracing was obtained. From this, the moment at which the radioactive sodium reached the groin could be estimated.

Findings. The increase in foot-groin time was fairly gradual and constant during pregnancy. The engagement of the fetal head seemed to cause a secondary obstruction to blood flow. The time at which this took place varied considerably in different women, occurring in some instances as early as the twenty-eighth week of gestation (in primiparas), while in multiparas it was usually delayed until labor was in progress.

The slowing of venous flow rate is confined to the legs and is not part of a generalized increase in circulation time. This slowing may be a factor in the onset of venous thrombosis.—*Mary Frances Vastine, M.D.*

Genitourinary System

Davis, David M. Diagnosis of renal tumors in the adult. *Radiology*, May, 1950, *54*, 639–645.

All renal neoplasms are regarded as malignant until proved otherwise. Biochemical methods of differentiating benign from malignant neoplasms are rather unreliable and difficult. Symptoms of hematuria, pain and palpable mass are evaluated. The greatest number of metastases occur in the lungs but may also be found in any other portion of the body.

Intravenous urography as a part of a routine examination is helpful, but when a renal tumor is seriously suspected, the author believes retrograde pyelography is the keystone in diagnosis. He also utilizes fluoroscopy to confirm the position of the catheter and to assure good filling.

The value of stereoscopic anteroposterior films is stressed. He does not recommend pneumopyelography. Filling of the ureter is important in ruling out ureteral tumors. Factors producing filling defects and the differential diagnosis are discussed.—*E. E. Seedorf, M.D.*

Geraci, Joseph E., Harris, Henry W., and Keith, Norman M. Bilateral diffuse nephrocalcinosis: report of two cases. *Proc. Staff Meet., Mayo Clin.*, June 7, 1950, *25*, 305–315.

Diffuse calcification of renal parenchyma has been noted in certain metabolic states, including hyperparathyroidism, vitamin D intoxication, hyperchloremic acidosis due to renal tubular dysfunction, and hypochloremic alkalosis associated with pyloric obstruction. It has also been seen in chronic or healed pyelonephritis, including that due to tuberculosis.

The authors present 2 cases with diffuse calcification of renal parenchyma, the process in each presumed to be the result of diffuse nephritis of long standing. A similar patient was reported in the literature a few years ago. In both their patients, the biochemical findings and clinical course led the authors to believe that the known metabolic states could be ruled out as possible etiologies. The authors' first patient, a man of forty-three with moderate renal insufficiency, had passed several renal calculi, and had had bouts of pyuria. He had had known very heavy diffuse bilateral calcification of the renal parenchyma for at least fifteen years, with only slight increase in calcific deposits over that period. This patient's films suggest that the heaviest calcific deposits are in the renal pyramids. The history of renal calculi and episodes of pyuria suggest a chronic pyelonephritic basis for the renal lesions.

The second patient, a man of fifty-two with uremia and severe hypertensive cardiovascular disease, showed a diffuse, symmetrical, finely granular calcification of the renal parenchyma bilaterally. At autopsy, the kidneys showed advanced chronic glomerulonephritis. Calcific deposits were seen in the renal tubular lumina, the tubular epithelium, and in edematous interstitial connective tissue. In this patient, as in the patient previously reported in the literature, there was a history of excessive intake of milk and dairy products during the time the glomerulonephritis may have been active.—*H. P. Brean, M.D.*

Beneventi, Francis A. Solitary pelvic kidney. *Urol. & Cutan. Rev.*, April, 1950, *54*, 201–206.

This is a presentation of a single case of solitary pelvic kidney demonstrated by cystoscopy and pyelogram in a male patient forty-eight years of age. The authors review the literature and tabulate the 44 cases which have been reported to date. The early reports in the nineteenth century were significant because the diagnosis was made only after removing the solitary organ, with a naturally fatal result. The diagnosis presently can be made by the deformity of the trigone as noted cystoscopically and

the demonstration on roentgenography of a pelvic kidney, usually with some deformity of the pelvis and calyces and with a short ureter.

The authors quote the work of Stevens (*J. Urol.*, 1937, *37*, 610) who has reviewed the previous literature and found that unilateral renal agenesis occurred once in every 700 to 1,600 autopsies and that 4 to 5 per cent of the single kidneys were true pelvic kidneys. Single true ectopic kidney occurs with equal frequency in males and females. It is two and one-half times more common on the right side than on the left. Symptoms are variable and often the condition is an incidental finding in the course of study as in the case herein reported.— *G. W. Chamberlin, M.D.*

Cayotte, Jacques. A propos de quelques difficultés du diagnostic des tumeurs malignes du rein. (Concerning some difficulties in the diagnosis of malignant tumors of the kidney.) *J. d'urol.*, 1950, *56*, 185–194.

Nine cases are reported, all eventually determined to be malignant renal neoplasms, each presenting difficulties in diagnosis due to misleading clinical and/or roentgenological features. The author emphasizes that the development of malignant tumors of the kidney may be extremely deceptive because of latent characteristics which often mask the gravity of the condition so that, when first seen, it is too late to operate with any chance of success.

Hemorrhage is regarded as one of the cardinal signs of renal cancer, and it is rarely absent. However, 3 of his cases had no hematuria, either gross, microscopic or by chemical tests and in 1 case bleeding was elicited only by pressure on the kidney.

In most cases roentgenological procedures yielded decisive findings when the diagnosis was in doubt, but in 2 the roentgen findings were so slight as to be only minor deviations from normal, and a diagnosis was possible only by evaluation of clinical and roentgen features. In 1 case, although there had been a history of hematuria, the only finding was of renal ptosis; when the patient was operated upon, with nephropexy contemplated, a wholly unsuspected parenchymal hypernephroma was found.

Caution must be exercised in evaluation of three roentgen findings which may, but do not necessarily, indicate neoplasm: (1) Upward elongation of a superior calyx is generally a simple anatomical arrangement and should not, of itself, serve as an argument or criterion for pathology. (2) A "claw arrangement" picture is indicative of one type of renal neoplasm, but is comparable to that seen in polycystic kidney; therefore both kidneys should be investigated by either retrograde or intravenous urography. (3) Lacunar shadows in the renal pelvis may indicate a blood clot. The pyelogram should be repeated after lavage of the renal pelvis.

In conclusion, the author states that it is necessary to undertake in all cases in which a diagnosis of renal cancer is suspected or in doubt, due either to insufficient signs or a misleading symptomatology, a most determined urological investigation. One must consider all findings, clinical, chemical, endoscopic, and roentgenological which, combined, are able to indicate an exact diagnosis.—*A. K. Wilson, M.D.*

Harvey, Rolfe M. Wilms' tumor; evaluation of treatment methods. *Radiology*, May, 1950, *54*, 689–699.

Wilms' tumor (embryonal adenosarcoma) comprises 20 per cent of malignant tumors in infancy and childhood. The embryonal nature of the tumor is emphasized. The different degrees of radiosensitivity of the tumor are dependent upon the proportion of embryonal sarcomatous cells to epithelial cells. The former are radiosensitive, the latter radioresistant.

Symptoms are usually lacking. The outstanding feature is an abdominal mass. Hematuria and pain are uncommon.

The diagnosis is based on finding an abdominal mass and eliminating other diseases by pyelography.

The literature has been reviewed in considering five basic plans of treatment of Wilms' tumor:

1. *Irradiation Alone.* The statement that no case of Wilms' tumor has ever been cured solely by roentgen therapy is commonly seen in the literature. However, several cases are cited who survived six to ten years following only irradiation. It is mentioned that this type of treatment is limited to inoperable cases, and cures, therefore, are not to be expected.

2. *Surgery Alone.* Ladd of Boston believes preoperative roentgen therapy is dangerous in that it permits metastases to develop during the treatment period. In his hands there were only 2 operative deaths in 37 consecutive nephrectomies.

3. *Preoperative Irradiation plus Surgery.* Large inoperable tumors shrink in size which makes removal easier, simultaneously reducing shock and lowering operative mortality. Irradiation inhibits growth by vascular obliteration. The delay during preoperative irradiation allows time to prepare the patient for surgery.

4. *Surgery plus Postoperative Irradiation.* The value of this method has been established by Neuhauser with a survival rate of 47.3 per cent reported.

5. *Preoperative Irradiation, Surgery, and Postoperative Irradiation.* Most commonly employed at present. Survival rate for this type of treatment surpasses all others.

Following a review of the statistical data from the literature, it is concluded that a large series of cases should be given the benefit of preoperative irradiation in addition to surgery and postoperative irradiation.—*E. E. Seedorf, M.D.*

Gondos, Béla. Ureteral calculus in relation to the border of the psoas muscle. *Urol. & Cutan. Rev.*, April, 1950, *54*, 196–201.

Five cases are presented to illustrate the author's observations that a stone stopped in the lumbar portion of the ureter not infrequently presents itself at the border of the psoas muscle. The long axis of these stones mostly conforms with that of the lateral border of the psoas muscle, and pyelographic studies indicate that the stones are located at the point where the ureter crosses the psoas muscle border. In the majority of instances, bowing or kinking of the ureter is demonstrable on the pyelograms and the ureter proximal to the bowing or kinking follows the psoas muscle border. Changes in the position of the stone in the upper ureter are most frequently in a retrograde direction. Spontaneous passage of a stone in such a ureter occurred only once in 14 cases seen by the author. It is not understood whether the kinked ureter is the primary factor in the arrest of the stone or whether the obstruction develops from peri-ureteral adhesions.

There is a suggestion in this paper that the physiology and pathology of the ureter may be affected by the psoas muscle.—*G. W. Chamberlin, M.D.*

Bottone, John J., Ittner, William F., and Santare, Vincent J. Bilateral ureteral obstruction caused by metastatic carcinoma; case report. *Urol. & Cutan. Rev.*, May, 1950, *54*, 266–269.

This is a report of an interesting and instructive case of a forty-eight year old white female with the chief complaint of anuria for twenty-four hours prior to admission to the hospital. Cystoscopic and retrograde pyelographic studies showed an almost complete block of the pelvic ureters. At operation this block was found to be due to a mass of matted, stony hard nodules completely surrounding both lower ureters below the brim of the bony pelvis. A biopsy was taken from these nodes and the ureters were transplanted to the skin. The histopathologic report was that of a metastatic carcinoma resembling the original breast tumor which this patient had had removed three years before. The patient subsequently developed recurrent nodules in the chest wall and on autopsy was found to have generalized carcinomatosis.—*G. W. Chamberlin, M.D.*

Ney, Charles, and Duff, John. Cystourethrography: its role in diagnosis of neurogenic bladder. *J. Urol.*, April, 1950, *63*, 640–652.

This article describes the various changes found in the bladder by cystography in cases of neurogenic bladder. The medium used by the authors was 4 per cent sodium iodide or 25–35 per cent neo-iopax. The dye was injected through a urethral catheter and anteroposterior film exposed. After this preliminary film with the bladder filled with dye a second film was exposed while dye was injected into the urethra with the bladder still filled. A third film was exposed in a 45 degree oblique position and additional films taken while voiding and after complete voiding.

The author describes the following changes which occur with neurogrenic bladder and illustrates these changes with film reproductions: (1) funnel urethra; (2) pine-tree shaped bladder; (3) vesico-ureteral reflux; (4) hour-glass bladder; (5) saccular dilatation of posterior urethra; (6) pseudo-sphincter formation; (7) spastic external sphincter; (8) relaxed external sphincter; (9) contracted hypertonic bladder; (10) large hypotonic bladder; (11) calculus formation.

The authors emphasize that no one of these changes is diagnostic of neurogenic bladder but their occurrence, especially in combinations of two or more, should lead to a careful neurological investigation.—*R. M. Harvey, M.D.*

Davidson, John A. Report of three cases of carcinoma occurring in exstrophy of the bladder. *Urol. & Cutan. Rev.*, April, 1950, *54*, 206–208.

Thirty cases of carcinoma occurring in exstrophy of the urinary bladder have been found in the literature. The authors herein report 3 patients, 2 having had a biopsy diagnosis, and 1 a clinical diagnosis of carcinoma in exstrophy. These 3 cases were found in a series of 23 instances of bladder exstrophy seen at the Duke Hospital since 1934. Nineteen of the 23 cases were under thirty years of age; the other 4 were between forty-seven and fifty-two, and all 3 patients who had a carcinoma complicating their exstrophy were in this latter age group.

Of the 3 cases presented showing carcinoma in exstrophy, 2 were lost to follow-up before treatment could be completed. The other case had a transplantation of the ureters, one into the sigmoid and one cutaneous with subsequent excision of the bladder. This patient had received roentgen therapy over the lesion without any benefit.—*G. W. Chamberlin, M.D.*

Gross, Robert E., and Moore, Thomas C. Duplication of the urethra; report of two cases and summary of the literature. *Arch. Surg.*, April, 1950, *60*, 749–761.

The authors review 81 cases of duplication of the urethra from the literature and add 2 cases of their own. All of the cases cited are apparently males. In 48 instances, the anomaly consisted of a blind accessory urethra opening on the upper side of the penis. Nineteen cases are reviewed in detail in which the accessory urethra arose independently in the bladder and extended to the dorsal surface of the penis. In 12 cases, the tract extended from the dorsal surface

of the penis to the normally placed urethra; 3 reports were of a blind accessory canal on the ventral penile surface; and 1 case was reviewed in which the anomalous urethra extended from the bladder to the normal urethra in the glans portion.

The cases which the authors submit are one of a blind ending dorsal accessory urethra and one of a complete accessory urethra.

The clinical significance of the condition is primarily that the accessory urethra is apt to harbor infections which are hard to eradicate. Also, the anomaly may considerably deform the penis and, in the case of complete accessory urethra, may produce incontinence.

Roentgen studies utilizing opaque solutions, catheters, or both, may be helpful in diagnosis. The authors describe the surgical correction of the various types of the anomaly.—*S. H. Fisher, M.D.*

Raines, Samuel I., and Maddux, Holt B. Sarcoma of the prostate; review of the literature and case report. *Urol. & Cutan. Rev.*, May, 1950, *54*, 283–287.

This condition is relatively rare but it is important because it is a challenge to the problem of early diagnosis. Sarcomas of the prostate are not infrequently confused with infection. The disease tends to occur in the younger age group, 30 per cent occurring in the first decade and 75 per cent before the age of forty. Sarcomas of fibrous tissue origin are the most common. Pleomorphic sarcoma of the prostate occurs next in frequency, followed by myosarcoma and then by lymphosarcoma. Metastasis through the lymphatics and the blood stream, as a rule, is not very extensive. The involvement of the bony pelvis usually occurs as a late complication and the lesions are of the osteolytic type. The acid phosphatase reaction is not elevated. The prognosis in most cases is poor, as most of the patients are first seen when the lesions are large and have already infiltrated the vesical neck. The differential diagnosis includes prostatic abscess, carcinoma, and frank prostatitis.

The authors report a case of a white male, aged forty-five, with an anaplastic sarcoma of the prostate which finally resulted in death from generalized tumor metastasis to the lungs, pleura, liver, adrenals, kidneys, retroperitoneal lymph nodes, and iliac bone.—*G. W. Chamberlin, M.D.*

Skeletal System

Thoman, William S., and Murphy, Robert E. Infantile cortical hyperostoses; a review of cases with a case report. *Radiology*, May, 1950, *54*, 735–740.

Clinically this disease is manifested by onset in infancy, irritability and fever, tenderness and swelling of face, jaws, scapula or extremities. Roentgenographically there is periosteal involvement or cortical hyperostosis in the following bones: mandible, clavicles, upper extremities, lower extremities, ribs, and scapulae in the order named.

There may also be leukocytosis, elevated alkaline phosphatase and elevated sedimentation rates.

The authors report the first case of an Indian infant with outstanding features of absence of irritability and involvement of the mandible, which is the most common site of involvement. There was a gradual regression of the lesions with no treatment beyond adequate diet.—*E. E. Seedorf, M.D.*

Haguenau, J., and Fauré, C. L'angiome vertébral. (Vertebral angioma.) *Presse méd.*, June 14, 1950, *58*, 675–677.

Hemangioma is one of the commonest benign tumors of the vertebrae, as reported by pathologists, occurring in about 10 per cent of spines examined. Clinical reports, on the other hand, suggest a rare occurrence. The reasons for this discrepancy may be that many of these tumors do not cause symptoms, and frequently ordinary roentgenographic methods do not demonstrate them. It is rare that an entire vertebra is involved. The tumor may be found in either the body of the vertebra or in the arch, often in a limited zone. Angiomas involving the posterior arch or the part of the body adjacent to the spinal canal may cause a spasmodic but progressive paraplegia, occasionally of sudden onset. Pain may be of the radicular or rheumatoid type. Rarely, hemangioma is revealed by spinal deformity, pulsating tumor in the vertebral region, signs of syringomyelia or the Brown-Sequard syndrome. The problem is not solved by clinical observation alone, by spinal fluid studies or by lipiodol which can only show a block. Only roentgenographic studies show a classical picture.

When a vertebral body is involved, its general morphology is usually not modified. Roentgenographically, there is an occasional swollen appearance in which the lateral borders become convex. The integrity of the adjacent discs is the important observation. Certain elements of the osseous trabeculation disappear and are replaced by angiomatous tissue, for the most part in a vertical direction. There is also a condensation reaction. The osseous tissues present an exaggerated transparency, an absence of homogeneity, and a riddled appearance of little holes separated by vertical partitions. The appearance has been described as "honey cake," "sponge," "pumice stone," and "tiger vertebra." The accent is on the vertical striation, best seen in profile view. With such a picture the diagnosis is easy. At times only a decalcified zone is observed. On the posterior arch, tomography may be necessary. Less common findings are homogeneous condensation, osteolytic collapse, and pseudo-Paget or pseudo-Pott's appearances. Other angiomas may be present, such as

epidural angioma, multiple osseous angiomas, or associated cutaneous, hepatic or splenic angioma. Pregnancy and endocrine factors may play a role because of the greater frequency in females and at puberty. The differential diagnosis involves Pott's disease, infectious spondylitis, syphilis, metastatic neoplasm, myeloma, lymphoblastoma, Paget's disease, actinomycosis, and echinococcus cyst.

Treatment is either surgery or roentgen therapy. Surgery consists of laminectomy for decompression of the compressed spinal cord. The angioma itself is not the object of surgery. The operation may be very sanguineous if the posterior arch is involved and the angioma is to be avoided if possible. With roentgen therapy the technique is to deliver from 2,000 to 3,000 r to the lesion. A posterior field and two anterior paramedian fields may be employed. Careful observation with a neurosurgeon is required if there is impending cord compression.

The results with surgery are fairly satisfactory. Poor results are due to tardy intervention. Roentgen therapy also produces favorable results even in those tumors producing cord compression. Pain may also be relieved by roentgen therapy but not too frequently. Radium therapy and the use of sclerosing solutions are now abandoned. If the tumor is symptomless, no treatment is indicated. In rapidly developing tumors with cord compression, surgery is indicated. Otherwise roentgen therapy is the treatment of choice. In the treatment of painful forms, immobilization in a plaster cast or rest in bed may be required while waiting for the effects of the roentgen therapy.—*S. M. Silverstone, M.D.*

Kurtz, Leonard, and duVigneaud, D. The lumbosacral joint in low back pain. *Alexander Blain Hosp. Bull.*, May, 1950, *9*, 138–150.

The authors believe that the vast majority of low back complaints are the result of lumbosacral instability with periodic decompensation of the lumbosacral ligaments and muscles. They discuss the anatomy and mechanics of the lumbosacral joint and the various factors leading to a change in normal mechanics and to the production of low back pain. The differential diagnosis, especially as regards ruptured intervertebral disc, is outlined as is the treatment for two groups of patients: (1) the fatigue or strain group and (2) the acute sprain group.

Four hundred and thirty-one patients with low back complaints were roentgenologically studied with respect to facet structure, weight thrust, lumbosacral angle, spondylolisthesis, posterior displacement of the fifth lumbar on the first sacral vertebra, transitional vertebrae, narrowing of the intervertebral spaces, and anomalous structures. One hundred and eight patients with no history of low back pain were studied as controls. From this study the authors conclude that any spine showing a lumbosacral angle greater than 49° and/or a weight thrust greater than 1.4 cm. has a probability of being potentially pathological in a ratio of 5:2. Posterior displacement of the fifth lumbar on the first sacral vertebra was found in 14.1 per cent of the pathological group and in 6.1 per cent of the control group. Anterior displacement or spondylolisthesis was found in 6.3 per cent of the abnormal group and 2.7 per cent of the normal group; however, 20 of the 26 cases of spondylolisthesis showed weight thrust greater than 1.5 cm. and/or a lumbosacral angle greater than 50°. If these factors indicate probable instability, it would seem reasonable to be cautious before blaming the low back pain on the spondylolisthesis per se. Seven and two-tenths per cent of the abnormal group showed suggestive narrowing of the intervertebral interspace as compared with 3.7 per cent in the normal group. Eight and one-tenth per cent of the abnormal group showed sacralization of the transverse process as compared to 4.6 per cent in the normal group. There were no conclusions of back stability from the slight difference in percentages as far as abnormality of the facets was concerned and asymmetry of the facets was found to be relatively unimportant.

The authors conclude that mechanical factors in the pathologic physiology of the lumbosacral joint are highly significant in establishing the etiology of low back pain.—*W. H. Smith, M.D.*

Shelton, George W., Garber, C. Zent, and Smith, Alan DeForest. Actinomycosis of the knee; report of a case. *Arch. Surg.*, April, 1950, *60*, 771–778.

A review of the literature by the authors fails to reveal any other case report of primary involvement of the knee joint with actinomycosis. They state that it is now generally believed that this disease is caused by an anaerobic organism present in the human mouth. Rarely, an aerobic organism found outside the body is the etiologic agent. A "hayseed" or "grass chewing" history is no longer important, whereas mouth and throat infections or human bites are of some significance. None of these factors, however, were present in this case and the authors were not able to demonstrate the portal of entry.

The case is that of a seventeen year old white girl who gave a history of injury to the right knee while swimming. She had immediate pain and swelling and limitation of motion, all of which subsided after a few days' rest, only to recur sporadically. Activity aggravated the symptoms and rest relieved them. On her first visit, about eight months after the injury, the right knee was slightly swollen and there was increased heat and tenderness along the medial joint line.

A roentgenogram taken at the first examination revealed swelling of the soft tissues about the right knee. There was no evidence of bone involvement. The complete blood count was normal. Mantoux and Kline tests gave negative reactions. The erythrocyte sedimentation rate was 78 mm. in one hour. An as-

piration of the knee was done and 30 cc. of dark red fluid was obtained. Yellow flecks were present in the fluid. Cultures and smears revealed microaerophilic and facultatively aerobic actinomyces resembling *Actinomyces bovis* and sulfur granules surrounded by polymorphonuclear leukocytes and a lesser number of large vacuolated mononuclear cells, red blood cells and small mononuclear cells.

After repeated aspirations, a synovectomy and multiple incisions and drainage for residual sinuses accompanied by the intramuscular and intra-articular injection of 76,000,000 units of penicillin, extending over a period of approximately a year, the patient gradually improved. On subsequent follow-up visits, the last of which was about three and a half years after her initial visit, there was full motion in the right knee, mild atrophy of the quadriceps muscle and no evidence of recurrence of the disease.—*H. H. Galston, M.D.*

Khoo, F. Y. Osteochondritis of the cuboid associated with tuberculosis of adjacent tarsal bones; report of a case. *J. Bone & Joint Surg.*, May, 1950, *32B*, 230–232.

This paper is a case report of osteochondritis of the cuboid with co-existing tuberculosis of the third cuneiform bone. The author believes that on the roentgenographic evidence the case reported was an actual occurrence of osteochondritis of the cuboid. He believes also that, from the clinical and roentgenographic findings and despite bacteriological proof, the lesions found in the patient elsewhere, namely, the left elbow, neck and chest, were tuberculous in nature. Evidence of widespread tuberculous involvement was further strengthened by the demonstration of calcified mesenteric nodes. In the left foot, beside a discharging sinus, there were patchy areas of destruction in the third cuneiform bone, which were considered to be tuberculous in origin.

The case seems remarkable for the fact that despite the presence of a slowly progressive tuberculous lesion of the third cuneiform bone, and possibly of contiguous structures, the osteochondritis of the cuboid went on to progressive recovery. It seems to the author that the tarsal osteochondritis and tuberculosis were two separate entities pursuing different courses in spite of their proximity to each other.—*R. S. Bromer, M.D.*

Pratt, Peyton T., Schwartz, Steven O., and Ehrlich, Lee. Aspiration biopsy of bone marrow as an aid in diagnosis of histoplasmosis; report of a case. *Arch. Int. Med.*, June, 1950, *85*, 893–899.

Because histoplasmosis is usually a systemic disease with many manifestations, its diagnosis is often difficult. The most frequent findings are splenomegaly, hepatomegaly, anemia, leukopenia, irregular elevations in temperature, pulmonary signs and symptoms, and oral lesions. In this situation the demonstration of the fungus as the etiological agent is necessary before a final diagnosis can be established. Where external lesions are present, the fungus may be demonstrated by culture or direct smear. In most of the cases reported to date, however, it was not possible to determine the diagnosis before autopsy. The authors report a case in which *Histoplasma capsulatum* was identified within abnormal histiocytes obtained by biopsy of the sternal marrow. The organism was identified on the smear of the marrow and also from cultures made from the marrow. As an incidental finding, a few abnormal cells were discovered in the peripheral blood which also contained the organism. This is a very unusual finding and cannot be depended upon for diagnosis. On the other hand, the presence of the organism in the bone marrow should be easily demonstrated in many of the obscure cases. For this reason, aspiration biopsy of the bone marrow should be considered as an important diagnostic aid in suspected cases of histoplasmosis.—*R. P. Barden, M.D.*

Blood and Lymph System

Euler, H. E. Technische Bemerkungen zur peroesophagealen Aortographie. (The technique of peresophageal aortography.) *Röntgen-Blätter*, May, 1950, *3*, 117–121.

The patient is given an injection of morphine-atropine and, after swabbing the pharynx with 2 per cent pantocaine, an esophagoscope with distal illumination is introduced under general anesthesia (usually evipan intravenously) 30 cm. from the alveolar ridge (the dental arch).

The site of the puncture is swabbed with 1 per cent trypaflavin and a cannula of 45 cm. length and a lumen of 4 mm. with a tip of 3.2 cm. length, 1.2 to 1.3 mm. external diameter and a lumen of 0.9 to 1.0 mm. is introduced dorsolaterally into the aortic lumen.

The injection of 30 to 70 cc. of uroselectan B or perabrodil (organic iodine compounds) in 50 to 80 per cent solution, is carried out by a device consisting of an oxygen bomb with a pressure ventil, connected to a container with sterile sodium chloride-rivanol solution, which in turn communicates with the syringe containing the opaque substance. A pressure up to 5 atmospheres is transmitted by opening a ventil from the bomb through the sodium chloride solution to the opaque medium, making possible a rapid injection without danger of air embolism.

Serial films in prone position with an automatic cassette changer, with short exposure time, and a Bucky diaphragm give a good visualization of the aorta and its branches and the small vessels of the abdominal organs. No complications were observed in the 42 cases examined by this method.—*K. E. Matzinger, M.D.*

Wagner, Frederick B., Jr., and Price, Alison H. Fatality after abdominal arteriography; prevention by new modification of technique. *Surgery*, April, 1950, *27*, 621–626

The authors reported 1 death in a series of 50 cases in which abdominal arteriography was used, and they attributed this death to an error in technique.

The patient was a white woman, aged forty-one, who had hypertensive cardiovascular disease, arteriosclerosis and conversion hysteria. A roentgenogram of the thorax revealed enlargement of the heart and a boot-shaped contour of its left border. It revealed pulmonary congestion and "lengthening with uncoiling of the aorta."

Translumbar abdominal arteriography was performed in an attempt to visualize the renal arteries and their branches. Ten cubic centimeters of an 80 per cent solution of sodium iodide was injected into the abdominal aorta within five seconds. The anesthetic was administered for three minutes and the arteriographic technique required two minutes. The arteriogram revealed that the needle had been inserted into the orifice of the superior mesenteric artery and that the entire amount of medium was dispersed throughout this vessel and its branches. Persistent abdominal pain, diffuse tenderness and rigidity developed. About six hours after the beginning of the injection, she was in a state of profound shock, and the blood pressure was unobtainable. The patient died, and death was ascribed to mesenteric thrombosis.

Because of this experience, the authors recommend that 10 cc. of a 30 per cent solution of sodium iodide be used initially and that a preliminary roentgenogram be made to determine whether the medium is in the desired site. If the puncture is satisfactory, the 80 per cent solution may then be injected.

The authors believe that vascular spasm together with the irritating effect of the concentrated solution of sodium iodide on the endothelium caused the diffuse thrombosis.

They observed 3 other cases in which the needle accidentally entered some vessel other than the aorta, but in these cases no untoward effects were noted. It is concluded that the safety of the patient and the success of abdominal arteriography depend upon an exact knowledge of the position of the needle prior to the injection of the medium.—*C. B. Holman, M.D.*

Dotter, Charles T., and Jackson, Frederic S. Death following angiocardiography. *Radiology*, April, 1950, *54*, 527–534.

In an effort to obtain a reliable estimate of the mortal dangers of angiocardiography a questionnaire was sent to many hospitals in the United States, Canada, Great Britain and Sweden. The authors tabulated the returns and found that death occurred in 26 out of 6,824 investigations (0.38 per cent).

In North America there was 1 death per 397 angiocardiograms while in Great Britain there was 1 in 59. Apparently the difference is due to the fact that the English doctors restrict the use of angiocardiography to patients with congenital heart disease while in America the examination is also used for other conditions.

The commonest cause of death was respiratory arrest immediately or shortly after the injection of the opaque medium. In spite of postmortem examinations, the immediate cause of death was rarely found.

Allergy, anesthesia or premedication did not seem to play a part in the sudden death. An unexplained finding was that there were very few deaths in the series when the patient was examined in the upright position.—*C. A. Stevenson, M.D.*

Schmidt, W., Schulte, A., and Lapp, H. Klinischer und pathologisch-anatomischer Beitrag zur Frage der Schädigung durch Thorotrast. (Clinical and pathologic-anatomic contributions to the question of injury from thorotrast.) *Strahlentherapie*, 1950, *81*, 93–102.

A man, aged thirty-five, was subjected to cerebral arteriography with thorotrast after a diagnosis of brain tumor. Subsequent study revealed that his symptoms were due to multiple sclerosis.

Ten years later the patient died with a profound panmyelopathy. At autopsy extensive deposits of thorotrast were demonstrated in the macrophages of the spleen, lymph nodes, liver and bone marrow.—*H. G. Moehring, M.D.*

Schrader, E. A. Die Arteriose der Arteria femoralis. (Arteriosis of the femoral artery.) *Deutsche med. Wchnschr.*, May, 1950, *75*, 670–674.

A new clinical and pathological entity characterized by a progressive obliteration of the femoral artery is described.

Thirty-five cases were observed, all males between forty-five and seventy-one years of age.

The symptoms were unilateral or bilateral dysbasis intermittens with absence of pulse of the arteria dorsalis pedis but without trophic changes. No signs of generalized vascular disease were present.

Arteriograms obtained by percutaneous injection of 70 cc. of 35 per cent perabrodil (an organic iodine compound) into the femoral artery below the inguinal ligament showed circumscribed obliteration of the femoral artery in the middle third with compensatory dilatation of the arteria profunda femoris anastomosing with the segment of the femoral artery, distal to the part affected. This anastomosis

is wide and good filling of the lower third of the femoral artery with the contrast substance is seen on all films. This explains the benign character of the disease and the absence of trophic changes.

The author tries to explain the location of this disease in the middle third of the femoral artery by the fact that the segment of the femoral artery above the anastomosis with the arteria profunda femoris is a locus minoris resistentiae having no anastomosis with other femoral vessels. The vasa vasorum in this segment are true end-arteries and their endarteritis leads to the obliterative process described.

Treatment consisted in resection of the diseased segment of the femoral artery by Leriche's method. Histopathological examination showed endarteritis obliterans.—*K. E. Matzinger, M.D.*

Barrett, N. R. Foreign bodies in the cardiovascular system. *Brit. J. Surg.*, April, 1950, *37*, 416–445.

This paper deals with solid foreign bodies which have come to rest in the cardiovascular system without immediately killing the patient. The author reviews selected parts of the quite extensive literature to describe the ways in which the blood channels can be penetrated; to report upon the vagaries of solid objects in the blood stream.

The literature abounds in hundreds of single case reports. Few are unique. Many of these cases are used as examples in the discussion. The general headings are as follows:

1. Foreign bodies may enter the venous system in several different ways.
   a. The patient is unaware of the accident.
   b. Fragments lodged in the liver are prone to enter the hepatic veins or the inferior vena cava.
   c. Foreign bodies penetrating a peripheral vein can enter the lumen and be carried away.
   d. A hypodermic needle or a piece of catheter may break off inside a vein.
   e. A fragment lodged partly inside and partly outside may break off and pass into the lumen.
   f. Erosion of the wall of a vein can be caused by radium needles lying adjacent.
   g. The cardiovascular system has been entered at the following sites from the alimentary canal: (1) pyriform fossa, (2) lower end of the esophagus, and (3) third part of the duodenum.
   h. Foreign bodies have entered veins from the uterus, vagina, bladder, and bronchial tree.
2. Foreign bodies can get into the pulmonary artery by direct penetration of the lung.
3. Foreign bodies generally get into systemic arteries as emboli from the left side of the heart, but there are records of missiles which have entered the aorta and other large vessels directly.
4. Foreign bodies found in the heart usually get there by direct perforation through the thorax; they may be situated in the pericardium, the myocardium or in a chamber of the heart. Foreign bodies in the right side of the heart or a branch of the pulmonary artery may have migrated from a peripheral vein. Those on the left side get there from a direct wound of the heart or pulmonary vein or by "paradoxical embolism" through a patent foramen ovale or interventricular septum.

These objects may migrate forward or in a retrograde manner depending upon their size, weight, shape, and consistency. The migration from a peripheral vein to the heart or pulmonary artery is usually symptomless, while migration from the left heart into a systemic artery may produce ischemia or gangrene.

A foreign body lodged in the cardiovascular system is always a potential danger to life and should be removed from wherever it is whenever possible. Symptoms and complications may be present from the first or they may not arise for months or years. In all cases they are likely to occur ultimately. When peripheral complications occur, the foreign bodies must be removed if there are no special difficulties or problems. When they are lodged in the heart, present-day surgical techniques are such that the onus is now upon the surgeon to say why a particular object should not be taken out of the heart rather than why an operation should be advised.—*Norman Heilbrun, M.D.*

Lindgren, E. Percutaneous angiography of the vertebral artery. *Acta radiol.*, May, 1950, *33*, 389–404.

Because the author did not regard the various methods for visualizing the vertebral artery as being entirely successful, he decided to approach this vessel from the front of the neck. In 1947, after having done 24 vertebral angiographies from the anterior approach he reported his method before the Swedish Society of Radiology. In 18 cases the vessels of the posterior fossa were satisfactorily visualized.

Under normal conditions the vertebral artery is accessible from the front but this is not always the case in pathologic states. Thus the puncture should be made fairly high in the neck where spondylous changes are less apt to occur. Compared to the carotid artery, the vertebral artery seems to be more fixed. The proper spot of puncture is selected after studying the plain films of the cervical spine. The frontal (anteroposterior) view will show the approximate position of the artery.

It is too early as yet to estimate how often the percutaneous puncture of the vertebral artery is successful. The author has found that the results depend largely on the skill and experience of the operator as well as upon the width of the vessel and on anomalies or other changes in the spinal column.

He estimates that the percutaneous puncture method is possible in about two-thirds of the cases.

To date the author has carried out a total of 60 such angiographies. Usually there is no discomfort to the patient. However, in this series of 60, one patient became blind for three days and another was in a dazed condition for twenty-four hours following the injection. The contrast medium employed in all cases was 35 per cent umbradil.—*Mary Frances Vastine, M.D.*

Rose, L. M. Hypertrophy of the lower limbs with cutaneous naevus and varicose veins. *Arch. Dis. Childhood*, June, 1950, *25*, 162–169.

This is an example of a syndrome described by Klippel and Trenaunay which is one of the hemangiectatic hypertrophies. The syndrome consists of: (1) a superficial nevus—usually of a lower limb; (2) varicosities of the veins on the same side as the nevus; and (3) hypertrophy of the affected lower limb, involving the soft and bony tissues (particularly the latter). The syndrome is closely related to diffuse phlebectasis or congenital varicose veins. The hemangioma is of the port wine or nodular type. The vascular dilatations vary from simple dilatations to true arteriovenous communications. The bone changes consist of lengthening and cortical thickening. There is a strong familial tendency.—*S. H. Fisher, M.D.*

Villafañe, Eugenio Puyó. Trombosis aortoilíaca. (Aortic and iliac thrombosis.) *Prensa méd. argent.*, July 28, 1950, *37*, 1710–1714.

This article first gives a historical and clinical review, with numerous references to other authors. There is an extensive bibliography. The diagnosis of aortic and iliac thrombosis is not difficult. Contrast roentgenography is useful but not an indispensable recourse. Furthermore, it is not a harmless procedure since there have been some unfavorable results with gangrene of rapid evolution or acquired fatal mesenteric thrombosis. This procedure is entirely contraindicated when and if there is some degree of cardiac insufficiency, edema, cyanosis and dyspnea.

The author discusses the symptoms of the different stages of the process, the initial stage, the period of compensated obliteration and finally the period of decompensated obliteration. The medical treatment can be only symptomatic. Theoretically the treatment should be surgical, based on four possible types of intervention: (1) arterial graft; (2) thromboarteriectomy; (3) arteriectomy; and (4) sympathectomy.—*J. T. Case, M.D.*

Tischendorf, W., and Heckner, F. Zur Zytologie und Klinik der grossfollikulären Lymphadenopathie (Brill-Symmerssche Krankheit). (The cytology and clinical findings of giant follicular lymphadenopathy [Brill-Symmers' disease].) *Neue med. Welt*, July 29, 1950, *1*, 1013–1018.

Giant follicular lymphadenopathy was first correctly identified by Brill *et al.* in 1925. Early the course is relatively benign with lymphadenopathy particularly cervical, and occasional splenomegaly. Later, skin changes, eosinophilia, hepatomegaly, mesenteric lymphadenopathy, ascites, pleural effusion, bone involvement and the general symptomatology of blood dyscrasias supervene. The usual laboratory findings are non-contributory and the diagnosis is made histopathologically. Huge follicles are seen in the lymph nodes with reticular hyperplasia in the presarcomatous phase and later the nodes have the appearance of lymphosarcoma, reticulum cell or giant cell sarcoma. The authors studied 2 clinical cases in detail and, using fresh material from the nodes, identified cells of epithelioid type, the cytology of which is characteristic. An extensive cytologic description of this is presented together with several photomicrographs. The involved lymph nodes are radiosensitive in doses of 600 to 800 r in the early phases of the disease but resistance occurs later, in the sarcomatous stage.—*L. A. Nash, M.D.*

General

Riley, W. Champ, and Gailland, Louis. Significance of anemia, leukopenia and Pel-Ebstein fever in Hodgkin's disease. *Arch. Int. Med.*, May, 1950, *85*, 795–805.

Primary involvement of deeper structures (10–30 per cent cases) in Hodgkin's disease presents a serious diagnostic problem.

The association of anemia, leukopenia and Pel-Ebstein fever in patients with Hodgkin's disease is rare and their significance has not been previously evaluated. A report of such a case is presented with the pathological and histologic findings and a tabulation of the previously reported cases. A discussion follows, with reports from the literature, on 70 per cent abdominal cases of Hodgkin's disease, the relationship of the Pel-Ebstein fever and the presence of the splenic enlargement, anemia and leukopenia. The possible relation to involvement of abdominal lymphoid structures is emphasized. The authors feel that this triad is not coincidental and, while rare, appears to be associated with involvement of the abdominal lymphoid structures.—*G. H. Ramsey, M.D.*

Wheeler, Warren E., Friedman, Valerie, and Saslow, Samuel. Simultaneous nonfatal systemic histoplasmosis in two cousins. *Am. J. Dis. Child.*, May, 1950, *79*, 806–819.

Up to 1946, only 75 cases of systemic histoplasmosis had been reported in the literature and the impression obtained was that this disease was uniformly fatal. The authors report 2 cases which represent instances of non-fatal systemic histoplasmosis with apparent recovery. The patients were boys, aged eight and five and a half years respectively. In the first case, the roentgenogram of the chest showed widely dispersed mottled, streaky infiltration throughout both pulmonary lung fields, denser in the bases aud hilar areas and fading off to the periphery. Both hilar areas showed knobby densities and there was fluid present in small quantity in the right pleural cavity. Serial roentgenograms showed later, clearing of the patchy infiltration in the periphery of the lung and the most recent films revealed calcification in the left hilar nodes.

The roentgen examination of the second case showed knobby hilar densities bilaterally and infiltration along both cardiac borders. The peripheries of the lungs were clear. Calcification shadows were present in the lungs of both the father and mother, but the patient's sister showed no abnormality of the lungs, on roentgen examination.

The clinical features exhibited by the two children showed no significant difference from those previously reported in fatal cases. The authors believe from their study of these and other cases that *Histoplasma* infections in children exhibit a varied severity of involvement. There are a few persons living in endemic areas who acquire a generalized infection with the fungus and die. During the infection the organism appears in the blood and bone marrow; the liver, spleen and lymph nodes are enlarged and there is often pulmonary infiltration. Usually the patient dies before the pulmonary infiltration clears and is replaced by calcification. A few other persons acquire similar infection but recover spontaneously. A few others, usually older children, show symptoms of pneumonitis but do not have the severe systemic involvement characteristic of infants. A large number of persons living in endemic areas probably acquire asymptomatic pulmonary infections which resolve with evidences of calcification. Whether all persons discovered to have positive reactions to histoplasmin tests and pulmonary calcifications represent instances of healed infections of the foregoing type is not clear. Some histoplasmin-positive persons show no calcium deposits in their lungs, a fact which leads to the speculation that sometimes the positive cutaneous reaction may reflect healed systemic lesions rather than healed pulmonary lesions.

The therapy of the authors' patients consisted essentially of rest in bed and a diet similar to that used for patients with tuberculosis. It is their considered opinion that none of the drugs used, streptomycin, sulfadiazine or penicillin, contributed significantly to their patients' recovery.—*R. S. Bromer, M.D.*

RADIATION THERAPY

Howell, J. B. Cancer of the center face. *South. M. J.*, April, 1950, *43*, 283–291.

This paper deals with the treatment of cutaneous cancer of the nose and periorbital region with interstitial implants of low intensity radium needles. The author states that this method is worthy of greater usage and more widespread popularity.

The advantages of this method are as follows: a lesion involving the entire nose may be needled properly without development of painful chondritis or necrosis of cartilage; the cosmetic results are good; dosage calculations are possible; the approximation of the radioactive sources to the cancer is more accurate; the lateral and downward extensions can be covered more adequately; silent extensions are less likely to occur since an area of 0.5 cm. beyond the needles in all directions receives cancerocidal dosage; owing to the minimal cartilage damage, the cure rate is high; and finally, large and infiltrating lesions can also be successfully treated.

The dose varies from approximately 6,000 to 12,000 gamma roentgens. The needles used have an active length of 0.5, 1.5 and 4.0 cm. and contain 0.66, 1.33 and 2.4 mg. of radium respectively. They are made of platinum iridium and have a wall thickness of 1.5 to 0.6 mm. and contain 0.66 mg. of radium per cm. of active length. For the inner canthus curved needles are used. All needles remain in situ for 168 hours.

The author states that any cancer, except the very superficial ones measuring approximately 1 cm. or less, should be treated by this method. He feels that for infiltrating lesions of the canthi and lids, roentgen therapy is inferior to low intensity radium needle therapy, since the inadequate depth dose often leads to recurrences. Lesions which have recurred following a cancerocidal dose of roentgen rays or radium and a lesion which has invaded the orbit to a degree which cannot be accurately estimated or to an extent beyond the range of the needles should not be treated by this method.

The untoward effects and hazards from radium used about the eye are discussed. The minimal dose of radiation capable of producing cataract is still unknown but the general impression is that the mature, adult lens possesses a high degree of resistance to irradiation. The average latent period is believed to be approximately two years. The author makes measurements of the distance between the lens and the radium and by using isodose curves can estimate the number of gamma roentgens the lens receives. The maximum amount received without correction for the time factor is approximately 1,000 to 740 gamma roentgens (535 to 399 with corrections). The incidence of cataract formation is small.

Nineteen epitheliomas of the nose were treated and one failure is reported. Fourteen epitheliomas

of the lids and canthi have been treated with no failures.

There are numerous photographs and diagrams and one table giving the dose delivered along the active length of the needles.—*J. G. Snead, M.D.*

Leroux-Robert, Jean. La chirurgie seule et l'association chirurgie-radiothérapie dans le traitement des épithéliomas du larynx et de l'hypopharynx; indications et résultats; (à propos de 400 interventions). (Surgery alone or a combination of surgery and radiotherapy in the treatment of cancer of the larynx and hypopharynx; indications and results; report of 400 cases.) *Ann. d'oto-laryng.*, April, 1950, *67*, 217–255.

This is a report on 407 cases of carcinoma of the larynx and hypopharynx treated in the last fourteen years either by surgery alone or surgery combined with radiation therapy. Two hundred of these have been followed for more than three years.

The first part of the study is devoted to the review of the various surgical procedures which can be performed, such as thyrotomies, partial laryngectomies, total laryngectomies, and pharyngo-laryngectomies, depending upon the extension of the disease.

Classification of the tumors is the one adopted many years ago by the French school and partially originated by the author. It distinguishes three levels of site of origin for the tumors of the larynx proper—tumors of the vocal cord; tumors of the subglottic region; tumors of the supraglottic region which originate on the ventricles, ventricular bands, the laryngeal aspect of the epiglottis, and aryepiglottic folds. Tumors of the pyriform sinus are to be considered separately, distinguishing two levels—the bottom of the pyriform sinus and the upper aspect of the aryepiglottic fold on the pyriform sinus side.

Due to the anaplasticity of the tumors of the supraglottic level, and their high percentage of lymph node involvement, routine postoperative roentgen therapy is given as soon as the wound is healed. The author emphasizes the fact that irradiation is more effective if given before the lymph nodes are palpable. This policy is based on the idea that small microscopic nests of cells are more radiosensitive than large, involved lymph nodes. The tumor dose given is moderately high, about 6,000 r in sixty days. If lymph nodes are palpable at the time of laryngectomy, simple removal of these nodes, or partial neck dissection, is performed and the author relies on roentgen therapy for sterilization of the microscopic neoplastic involvement.

In the subglottic tumors, routine postoperative roentgen therapy is not given but is reserved for cases in which the histopathological examination of the operative specimen does not show enough clearance around the cut surface.

For tumors extending down in the direction of the hypopharynx and for tumors of the pyriform sinus, a pharyngo-laryngectomy is performed with continuity dissection of the involved lymph nodes, if present at the time of operation. If no lymph nodes are present, radical neck dissection is not done routinely. Roentgen therapy is usually given as soon as the surgical wound is healed, that is to say, around the twentieth to twenty-fifth day following operation, no matter whether or not neck dissection has been done. The author emphasizes the necessity of having all radical neck dissections followed by routine postoperative irradiation. In certain instances, following partially successful roentgen therapy which has shrunk the lesion, laryngo-oropharyngectomy, can be performed.

Several tables give the results of the various types of procedures, and from different viewpoints. These tables bring out, in particular, the fact that three year results are quite satisfactory for evaluation of methods as there is little difference between the three and five year results if one takes into account the normal mortality rate.

The results for early types of tumors, mostly those involving the vocal cords, are those of surgery alone. Interesting for the radiotherapist are the results produced by surgery followed by roentgen therapy in tumors of the vestibule and pyriform sinus. The author states that he has never cured, by surgery alone, an advanced case of tumor of the vestibule or aryepiglottic fold and that a combination of surgery and postoperative irradiation has given 15 cures in 50 cases, or 30 per cent. He also states that, in his hands (and according to the literature), it has been the exception that pyriform sinus tumors have been cured by either radiation alone or surgery alone, whereas an association of the two methods has yielded 6 cures in 27 cases, or 22 per cent.

Finally, the complications and functional results of the various types of procedures are reviewed.

The author, who works at the Curie Foundation in close cooperation with the radiotherapists, is an outstanding laryngologist specializing in tumors of the larynx and pharynx. This study has a wealth of information which cannot be given in an abstract and it is highly recommended that the paper be read by all those interested in the treatment of laryngeal tumors.—*G. H. Fletcher, M.D.*

Orr, Thomas G. An attempt to evaluate the radical and palliative treatment of breast carcinoma. *Surg., Gynec. & Obst.*, April, 1950, *90*, 413–422.

In his discussion of radiation therapy the author states that this treatment has been generally accepted in cases of advanced breast carcinoma.

Suffering is relieved and life is prolonged by the use of the roentgen rays in these patients. Any surgeon who has seen such a case treated in this manner must reason that cancer cells existing beyond or remaining in the operative field after the radical operation may be devitalized or destroyed by the roentgen rays. If this viewpoint is accepted, postoperative irradiation is indicated in all cases in which there is a reasonable possibility that cancer has not been removed completely by operation.

Since estrogens have been shown to increase the growth of breast cancer experimentally and their therapeutic use to increase the rapidity of cancer growth, it is reasonable to believe that castration may be of value in the treatment of patients before the menopause. Since castration is never curative and is only temporarily beneficial, routine castration in all patients of premenopausal age with breast cancer should not be recommended.

Treatment of breast cancer with sex hormones may be palliative but is never curative. The best results have been obtained with testosterone. When given in advanced cases in relatively high dosage, favorable and worthwhile palliation is often obtained.

In the final discussion and conclusions, the following points are made:

1. The value of surgical treatment of breast carcinoma cannot be estimated accurately. Grading of breast carcinoma to estimate the prognosis has not proved of great importance.

2. All types of therapy for carcinoma of the breast, except surgical, must be considered palliative. Since no one knows the percentage of cures that may be expected from surgical therapy, the term "survivals" is more in keeping with our present knowledge of the natural history of the disease.

3. If we accept irradiation as valuable treatment for inoperable cancer of the breast, it would be illogical to assume that such treatment would be without merit as an adjunct to surgical therapy.

4. Possibly more radical surgery in the future may salvage a very small percentage of breast carcinomas now considered incurable. It is evident that there are many problems relating to the treatment of carcinoma of the breast which remain unsolved. "To champion one method of treatment or technique of operation to the exclusion of all others may smack of dogmatism and dogmatism never does much toward the solving of scientific problems."—*Mary Frances Vastine, M.D.*

Percival, Eleanor, and Campbell, Archibald D. The status of radiation therapy in carcinoma of the cervix. *Canad. M.A.J.*, April, 1950, *62*, 335–338.

The series of cases presented by the authors comprises 261 consecutive cases of primary carcinoma of the cervix treated at the Montreal General Hospital in the ten year period between 1934 and 1943. All cases are proved histopathologically and are arranged in four clinical groups according to the Schmitz classification. In this grouping it was found that 63 per cent of the cases were advanced when first seen, that is, Stage III and Stage IV.

Treatment in all, except Stage IV cases, consisted of both deep roentgen therapy and radium application. It is emphasized that the treatment, particularly the radium application, is individualized. The radium is inserted in the uterus and in the cervical canal, against the tumor and in each lateral fornix. The radium, screened by 2 mm. brass and 3 mm. rubber, is administered in two treatments ten days apart, to give a total dose varying from 4,500 to 6,000 milligram hours. (The gamma roentgen distribution is not specified.) The treatment is done under general anesthesia, with great care being taken to place the radium accurately and to protect the rectum and bladder by tight vaginal packing and catheter drainage of the bladder. The radium treatment is followed immediately by deep roentgen therapy. If difficulty in locating the cervical canal is anticipated or if the tumor is large and infected, then roentgen therapy precedes the insertion of radium. When radium therapy is employed first, an antibiotic powder is insufflated into the vagina for two days before treatment to lessen the infection. Roentgen therapy is administered through four ports of 150 sq. cm. with 200 kv., filtered through 0.5 mm. of copper to give a total dose of 1,750 to 2,250 roentgens, measured in air.

The results of treatment show an over-all five year salvage of 43.2 per cent. Prognosis depends very largely on the extent of the disease when first treated as is seen when the results of all Stage I and Stage II cases are added, giving a combined salvage (five years) of 73.9 per cent. This is contrasted with a combined five year salvage of the cases of Stage III and Stage IV amounting to 25.4 per cent. Neither age nor pathological grouping appreciably alter the prognosis. Up to sixty years of age there is no material difference and over sixty the diminished salvage is due to death from other causes. Of the group, 6.5 per cent showed adenocarcinoma, and the figures of these are the same as in the epidermoid group. The ten year results in 134 cases from 1934 to 1938 show a salvage of 29.8 per cent. A comparison of the present series with a previous one of 200 cases treated from 1926 to 1933 shows an improvement of 16 per cent in the more recent group. This the authors attribute to the more individualized radium treatment done under the supervision of one person to improved higher voltage roentgen therapy, and to more adequate social service follow-up of the patients. Also mentioned is the fact that since 1934 all cases, even the early ones with no parametrial involvement, received a full series of roentgen treatments. This seems of equal importance to the above mentioned factors.

The authors also discuss the possibilities for

improving the results in the future. They give reasons for stating that the continued use of radium and roentgen therapy rather than spectacular but debilitating surgery offers the better prospects. Education by cancer campaigns emphasizing the necessity of early diagnosis as well as of the fact that even those cases that are not early have a significant hope for cure is recommended. More hospital beds should be set aside for carcinoma cases and no delay should be necessary in admitting suspected or frank cases. By further study of cell response to the gamma ray, those tumors which are resistant to radiation on histopathological and cytological grounds should be selected for surgery. The use of higher voltage roentgen therapy and of the newer isotopes may do much to increase the survival rate.—*H. H. Galston, M.D.*

Taylor, Grantley Walder. Surgical management of cervical lymph node metastases. *Radiology*, July, 1950, *55*, 60–61.

Every case of malignant neoplasm about the head and neck must be evaluated in regard to possible metastases to cervical lymph nodes.

Before treatment of the lymph nodes is undertaken, the primary carcinoma must have been controlled or must be controllable. Regional lymph node dissection is undertaken for obvious metastasis, and also when there is a high degree of probability of metastases. The extent of dissection is based on the zones of lymphatic drainage involved. Dissections are performed, as a rule, two to six weeks after treatment of the primary lesion.

In 100 cases of cancer of the lip in which the primary lesion was cured there were 58 per cent cures after dissection of positive lymph nodes. Dissection of positive lymph nodes from a primary cancer of the tongue showed 43 per cent cures and from a primary carcinoma in other parts of the mouth 38 per cent cures

In recent years improved anesthesia, chemotherapy and antibiotics have resulted in renewed interest in one stage en bloc operations. No critical evaluation of these procedures is possible at present. —*A. W. Sommer, M.D.*

Lear, Harold, and Oppenheimer, Gordon D. Anuria following radiation therapy in leukemia. *J.A.M.A.*, July 1, 1950, *143*, 806–807.

A case of chronic lymphatic leukemia in a white male, aged sixty-one, was treated with radiation therapy. On admission, the white cell count was 475,000 per cubic millimeter, with 94 per cent lymphocytes. After twelve days of total body irradiation with 50 r anteriorly and posteriorly, the patient's white blood cells numbered 45,000 per cubic millimeter. Two days later the patient was admitted to the hospital with complaints of anuria, nausea, and vomiting for twenty-four hours.

Investigation showed that both upper urinary tracts were completely filled with uric acid crystals. The blood uric acid level was 15.8 mg. per cent. The patient died of severe pyelonephritis and septicemia.

The authors explain the evolution of this case on the fact that the rapid destruction of nucleoproteins as reflected in the rapid drop of the white blood cell count caused an increase in the uric acid metabolism of the body. This caused an elevation of the blood uric acid, anuria, and crystalluria.

The authors recommend preliminary blood uric acid and renal studies in such cases before therapy is instituted. Precipitous destruction of white cells should be guarded against.

If proper precautions are taken the authors believe that complications such as occurred in the case cited here might reasonably be avoided.—*H. J. Thompson, Jr., M.D.*

McLaren, Hugh C. Ill effects of the radium menopause. *Brit. M. J.*, July 8, 1950, *2*, 76–80.

In view of the number of cases of non-malignant uterine bleeding which are treated by artificial induction of the menopause with application of intrauterine radium, this author has reviewed the immediate and remote sequelae of such treatment.

Varying numbers of cases were examined and interviewed approximately two years following intrauterine radium therapy (2,400 mg. hr.). The most striking findings were flushing and sweating, loss of libido, and premature senile changes in the genital tract.

One hundred and eighteen patients were reviewed in regard to flushing and it was found that severe and persistent attacks of flushing occurred about three times as frequently in this group as they did following normal menopause and in approximately the same percentage as following surgical castration.

Of 143 patients interviewed, 50 per cent had no sexual urge prior to the time that treatment was given. Of the group with normal libido 71 per cent suffered marked decrease or total loss of sexual desire following intrauterine radium. Fifty per cent of the group who previous to radium therapy had orgasm were unable to achieve this following treatment. Ten per cent developed dyspareunia. The author comments on the difficulty of obtaining accurate information concerning this phase of symptoms and regrets the absence of adequate control studies following normal menopause.

Premature aging of the genital tract, as studied by vaginal examination and vaginal smears, showed gross changes in approximately the same percentage as following surgical castration. The smears showed a varying number of senile cells in 70 per cent of the 68 cases studied.

In the light of these findings, the author recommends a conservative approach to metropathia with emphasis on systemic treatment. If radium or surgery is utilized, the patient should have adequate follow-up and hormonal therapy to relieve the symptoms which will follow in a majority of cases.—*Robert Emerick, M.D.*

Davies, C. E. Modern methods of treatment for malignant tumours of the eye. *Canad. M. A. J.*, June, 1950, *62*, 568–571.

Melanomas of the iris usually grow slowly in youth and later spread over the iris and into the ciliary body with consequent glaucoma. If the only area of involvement is around the pupil, a wide iridectomy can be done. When the iris base is involved, enucleation with radium bomb is the preferred method.

Choroidal nevi are usually located near the posterior pole of the eye. They are circular with feathered edges and blue or slate-gray in color. They should be carefully observed as malignancy may develop.

Melanomas of the choroid first appear in the outer layer of the choroid and then mushroom forward, detaching the retina, and the subretinal space is filled with albuminous fluid. Davies prefers enucleation with a long optic stalk and insertion of a radium bomb immediately.

Conjunctival nevi rarely become malignant. The tumors should be excised widely and beta radiation applied; with evidence of extension, enucleation with radium application is indicated.

Retinoblastoma arises from primitive cell rests and usually occurs in infancy or early childhood. The incidence of bilateral involvement is high—at least 25 per cent. Enucleation is done if only one eye is affected. Since extension occurs along the nerve, it is advisable to have the nerve cut distal to the chiasma and pushed into the orbit and followed with enucleation and removal of the entire nerve.

With bilateral retinoblastoma, after enucleation of the more involved eye, intensive irradiation should be given the opposite eye. Davies quotes Reese, Merriam and Martin who treated bilateral retinoblastoma with roentgen rays using small fields and heavy dosage with excellent results (see *Am. J. Ophth.*, 1949, *32*, 175).

Carcinoma of the eye is usually metastatic and Davies believes active treatment is not indicated. He reports 7 cases.—*Martha E. Mottram, M.D.*

Glucksmann, A. The role of the tumour bed in the treatment of squamous-cell cancers by irradiation. *J. Obst. & Gynaec. Brit. Emp.*, June, 1950, *57*, 322–327.

In this article from the Strangeways Research Laboratory in Cambridge, the author attempts to examine the facts related to the concept that differences in behavior of various irradiated squamous cell lesions may be attributable to differences in the tumor bed. For this purpose, he divides the tumor bed into two structures: (1) the distal tumor bed, which is the mesenchymatous tissue within which a primary or secondary lesion occurs, and (2) the proximal tumor bed which is the vascular, round cell, and oftentimes the subsequent fibrous stroma induced specifically by the given tumor. Multiple biopsies of primary lesions in the cervix, vagina, and vulva before and after radiation therapy are presented, and the clinical responses correlated with histopathological changes. Good tumor regression was seen in lesions where the major changes were visualized in the proximal tumor bed but when viable tumor cells remained, subsequent local recurrence was observed. Good long-term clinical results were obtained, however, when a profound response occurred in the tumor cells themselves, even in the absence of appreciable change in the appearance of the proximal tumor bed.

Survival figures are presented on 249 published cases of carcinoma of the oral cavity which received radiation therapy only after the regional lymph nodes had become involved. Of the failures, persistent tumor was found in the primary lesions with a frequency similar to that found in the lymph nodes, thus suggesting that the unfavorable response depended upon the peculiarities of the tumor itself more than upon the nature of the distal tumor bed. This was further borne out by the results of transplanting tumor tissue into the brains and subcutaneous tissues of young mice and observing identical responses to irradiation in the two localities. In this experiment, however, it was observed that the integrity of the vascular component of the proximal tumor bed in the grafts was definitely related to the radiation response.

The author concludes that the proximal tumor bed rather than the distal tumor bed plays a role in successful radiation therapy, but that the main feature is the capacity of the cancer cells themselves to react to irradiation.—*J. A. Martin, M.D.*

Wittenborg, Martin H. Roentgen therapy in neuroblastoma; a review of seventy-three cases. *Radiology*, May, 1950, *54*, 679–688.

Of the series of 73 patients having proved neuroblastomas, 80 per cent occurred within the first five years of life. The tumors occur most frequently in the upper abdomen, next most frequently in the pelvis. In 60 per cent of the patients, the tumor had already metastasized at the time of diagnosis. With skeletal metastases, death uniformly occurred within a year. Metastasis to the liver, however, offers an excellent prognosis if treated by irradiation.

Of the 73 patients, 28 had no specific therapy and 12 had surgery only. These cases are not discussed in detail. Roentgen therapy was administered to 11

patients following surgical treatment. In this group of patients with localized neuroblastoma there was a 66 per cent three year survival following postoperative irradiation. Twenty-two patients had biopsy and irradiation alone. Only 1 patient of this group was free of metastasis. The three year survival rate was 27 per cent

The technique of irradiation used varied considerably. It was found that almost all of the patients who survived without complications of treatment received initial tumor doses of 800 to 1,200 r in ten to fourteen days, usually followed by a second comparable series in three months. It is pointed out that immediate postoperative roentgen therapy with air doses to the skin of 1,400 and 1,800 r in seven to ten days causes no complication in the healing of the incision. The limiting dosage factor is not the skin, but the response of the hematopoietic tissues, especially where both the chest and abdomen are irradiated.—*E. M. Cooper, M.D.*

Mayor, G. Zur Therapie der infiltrierenden Blasentumoren. (Therapy of infiltrating tumors of the bladder.) *Schweiz. med. Wchnschr.*, Aug. 26, 1950, *80*, 900–902.

The author relates his experience with 55 tumors of the bladder observed in the surgical clinic of the University of Zürich since 1946. The histological distribution was as follows: Group I: Papillary fibroepithelioma (benign papilloma) 30 per cent; Group II: Papillary fibroepithelioma with atypical cells (malignant papilloma) 22 per cent; Group III: (a) papilliform carcinoma, (b) solid carcinoma, and (c) adenocarcinoma 48 per cent.

Of 16 cases of benign bladder tumors 12 were fulgurated and in 4 transvesical resection was carried out. Six developed a small recurrence which required usually one and only rarely two coagulations. All these patients are now well and are cystoscoped annually.

In 12 patients of the second group transvesical resection was carried out in 4; the remaining 8 were treated by transurethral coagulation. In 8 instances a recurrence developed but only one occurred in the resected cases. Of these 12 patients, 6 are now well; that means they are free from recurrence for over one year. Two others are also well but the observation period is less than one year; 1 patient died from myocarditis while in the hospital and the remaining 3 patients had complications: 2 a recurrence in the region of the ureteral orifices and hydronephrotic kidney, 1 a local recurrence complicated by the development of a hypernephroma which was treated by nephrectomy early in 1950.

The 27 cases of malignant bladder tumors are grouped as follows: (A) favorable patients. Only 6 of these (23 per cent) were well at the time of the report (2 for four years, 1 for three years, 2 for two years, 1 for eighteen months). In all of these a wide resection was carried out. (B) Nine patients died (35 per cent). All had inoperable tumors with local metastases. Three were treated conservatively, 3 by fulguration and 3 by resection. (C) Twelve patients are still under observation. Two of these are given as case reports in the article; 5 have been treated conservatively so far since they refused operation. In 5 resected cases 5 recurrences occurred. The author states that all cases of solid carcinoma and adenocarcinoma have a poor prognosis even when a very radical resection is carried out. The prognosis apparently depends not only on the histopathological character of the tumor but also upon the degree of the infiltrating process in the bladder wall. Whenever possible, wide resection should be carried out. Resection in inoperable cases combined with coagulation is not recommended. All patients had been under treatment for over a year since the first bladder symptoms. It is most important that these patients are seen and diagnosed early. More than half of all cases were inoperable upon admission. The general prognosis of infiltrating bladder tumors is poor. Radical operation should be performed as early as possible; he recommends cystectomy followed by implantation of the ureters. Indications for cystectomy are discussed in detail and the various surgical procedures as practiced in the author's clinic are described.

The use of radioactive isotopes, especially I^{131} and P^{32}, is also under investigation. $Cobalt^{60}$ has been used by Müller, who developed a special balloon which carries the isotopes in the form of the chloride of Co^{60} dissolved in water. The author treated one patient with this method in July, 1949; two months later the tumor in the bladder had disappeared. No final conclusions are possible because of the short observation period.—*E. A. Pohle, M.D.*

Arneson, A. N. Cancer of the cervix uteri; introduction. *Radiology*, June, 1950, *54*, 803–804.

The aim of this symposium was to present the problems arising with the more frequent diagnosis of pre-invasive cancer of the cervix uteri. The symposium also attempted to evaluate the therapeutic measures now available for adequate treatment of the local lesion as well as the normal pathways of spread for cervical cancer.—*E. M. Cooper, M.D.*

Galvin, Gerald A. Cancer of the cervix uteri; diagnosis of cancer of the cervix: the early lesion. *Radiology*, June, 1950, *54*, 804–812.

Intra-epithelial carcinoma is a lesion of the surface epithelium of the cervix in which the cells possess all the morphological and staining qualities of malignant cells but have not developed the powers of invasion. The epithelial cells are more or less of the same type and possess the criteria of malignancy in their cellular outline, their staining characteris-

tics and the irregularity and anaplasia of their nuclei.

Intra-epithelial carcinoma is the precursor of invasive carcinoma of the cervix, according to present day concepts. Diagnosis of this lesion is not difficult if the clinician and pathologist are aware that any abnormal cervix may harbor a latent carcinoma. It occurs in a relatively young age group, displays no pathognomonic signs and symptoms and can be completely eradicated. It can be detected only on biopsy or cytological smear. The author's experience with cytologic examination of the cervical smear has not been too encouraging, and he prefers cervical biopsies. Locke's doctrine, that the number of non-invasive carcinomas detected will be in proportion to the number of biopsies taken, is endorsed by the author. Repeat biopsies are advised in cases showing a "simple atypical epithelium" which does not follow the true intra-epithelial cancer picture.

One case is cited of a far advanced cancer of the cervix in which re-examination of a cervical biopsy specimen taken six years before revealed intra-epithelial cancer. Seventeen similar cases were found on review of medical literature.—*A. W. Sommer, M.D.*

Henriksen, Erle. Cancer of the cervix uteri; dispersion of cancer of the cervix. *Radiology*, June, 1950, *54*, 812–815.

Cancer of the cervis uteri may spread by the lymphatic channels, direct extension, or by distant metastases. Local lymphatic spread is to the paracervical, ureteral, obturator, hypogastric, external iliac, common iliac, aortic, sacral, and inguinal nodes.

The spread of cervical carcinoma by direct extension is to the bladder, rectum, vaginal walls, and the parametria.

Distant metastases occur earlier and more frequently than is usually believed with possible wide dissemination of this disease to the skin of the chest, axillary nodes, cervical nodes, pituitary gland, parotid gland, and the left supraclavicular nodes. The liver, vertebrae, and the pelvic bones are the most frequent sites of distant metastases.—*E. M. Cooper, M.D.*

Galvin, Gerald A. Cancer of the cervix uteri; classification of cervical cancer. *Radiology*, June, 1950, *54*, 815–819.

The various methods of classifying carcinoma of the cervix were devised in an attempt to facilitate the choice of therapy. These classifications of cervical cancers include the following: their amenability to surgery; their gross morphology; their histopathological characteristics; and their anatomical extension.

Only the anatomical spread of cervical cancer can be universally used as a basis of classification and the League of Nations classification approaches the ideal method. The author feels that a separate group must be created to include only the early microscopic cervical cancer.—*E. M. Cooper, M.D.*

Henriksen, Erle. Cancer of the cervix uteri; surgical treatment of cancer of the cervix. *Radiology*, June, 1950, *54*, 819–821.

Although radiotherapy is the method of choice in the treatment of cancer of the cervix, careful individualization of the case will often permit better results by surgery than by irradiation. The success of surgery depends on the correct estimate of the clinical stage of the disease.

For the so-called carcinoma in situ, or clinical Stage O, the author subscribes to the radical total hysterectomy as advocated by TeLinde. Here the ovaries, a little of the parametrium, and none of the nodes are removed. If the estimate of the disease is correct, the cure is certain.

For carefully selected cases in the Stage I and early Stage II groups, Meigs performs a radical total hysterectomy, with removal of the regional lymph nodes. The author suggests this type of treatment for those cases proved to be radioresistant.

Brunschwig's exenteration operation is offered as a means to lessen the effects of the extension of the disease within the pelvis. There are few men capable of performing this procedure which is a tremendous and physiologically mutilating operation.

Surgery and radiotherapy represent our only therapeutic devices and should be used together in order to improve our salvage rate of cancer of the cervix.—*E. M. Cooper, M.D.*

Nolan, James F., Costolow, William E., and DuSault, Lucille. Cancer of the cervix uteri; radium treatment of carcinoma of the cervix uteri. *Radiology*, June, 1950, *54*, 821–831.

Limitations of radium therapy for carcinoma of the cervix uteri are discussed and basic techniques are compared. Results are evaluated on the basis of dosage distribution. Six different techniques are compared, with accompanying diagrams to show radiation distribution. Techniques ranged from the use of three radium tubes in tandem in the uterine cavity to the Neary applicator. Conclusions are that none of the six techniques discussed are efficient enough to control cancer cells at a point of 5 cm. lateral to the midline in the approximate lymphatic drainage field adjacent to the pelvic wall. Only the Neary applicator reaches the 4,000 gamma roentgen level at this point, but this gain in efficiency is accompanied by a dangerous frequency of bowel injuries. A dosage of 4,000 gamma roentgens is considered the minimum adequate dose for tumor cell control.

Statistics are given covering 583 confirmed cases

treated at the Los Angeles Tumor Institute. Absolute five year survival for all primary cases was 41 per cent; Stage I, 73 per cent; Stage II, 50 per cent; Stage III, 28 per cent; Stage IV, 0 per cent.

Usual Method of Treatment: External roentgen therapy—1,800 r (air) to each of four pelvic portals, 10×15 cm. Factors: 450 kv., 1 mm. Pb filter, 50 cm. target skin distance, 5 mm. Cu half-value layer, 150 r (air) to 2 portals daily.

Intracavity Radium: Intrauterine tandem; two 25 mg. sources, 1 mm. Pt filter, 5.5 cm. length—2,600 mg. hour exposure.

Intravaginal Bomb: Three 25 mg. sources, 2 mm. Pt filter 1×2×3 cm. dimensions—2,600 mg. hour exposure, 2 or 3 treatments two to three weeks apart.

Graphs are presented to support the conclusion that increased dosage in Stage I does not bring about enough improvement in results to offset the effects of overdosage in the region of the parametrial triangle. It is for this reason that the Manchester group advocate the use of radium alone in the treatment of the early stages of the disease.

In cases classified as Stage II, where the disease may have reached the lymphatic drainage area, vigorous intracavity radiation is required. There is no significant variation in results regardless of intensity of radiation delivered to the lymphatic drainage area.

In Stage III the necessity for complete treatment probably outweighs the deleterious effects of high dosage. Graphs show that intracavity radiation and dose to the lymphatic drainage area must be adequate for tumor control.

Investigations tend to indicate a dependence of result upon the amount of radiation delivered to the lymph node-bearing areas when they are involved by disease. Therefore the concept of the ineffectiveness of radiation therapy in the treatment of involved pelvic lymph nodes is questioned.—*A. W. Sommer, M.D.*

Fletcher, Gilbert H. Cancer of the cervix uteri; roentgen treatment of cancer of the cervix. *Radiology*, June, 1950, *54*, 832–842.

The possibility of cure in cancer of the cervix is based on delivery of a tumor control dose to the whole tumor-bearing area. Radium or intravaginal therapy, correctly applied, can control primary cervical carcinoma, extensions to the fornices and lateral extensions of the tumor up to a certain distance from the midline. Lateral to this is a zone which will require additional irradiation, to supplement the radium dosage and to treat the lateral aspects of the parametrium and the pelvic lymph nodes. A minimum tumor dose of at least 5,000 r must be delivered to the lymph node-bearing area, added to whatever is received from the radium.

Carefully worked out volume distribution calculations and charting should be done routinely in the planning of roentgen therapy for each individual case.

The technique used by the author obtains a homogeneous irradiation of the lymph node area by cross firing through anterior, perineal, gluteal and sacral fields, using compression cones to improve depth dose. Fields are kept as small as possible. The midline and paracervical tissues should never be in the beam of the external rays once they have been adequately irradiated by radium.

Author's treatment factors: 400 kv., Thoraeus filter, 3 mm. Cu equivalent; half-value layer 4.2 mm. Cu; target-skin distance 66 cm. Doses of 300 r to 400 r (air dose) are given to two portals daily and a total of 4,000 r is given to each field. Over-all time of treatment is eight or nine weeks.

Doses given with this technique are higher than those given before. It represents an attempt to give higher dosage to the lateral aspects of the parametrium and to the pelvic lymph nodes. Despite the higher dosage level, no claim is made that metastatic carcinoma in the lymph nodes will be cured. Complications to be expected are local necrosis and marked fibrosis of the vagina, bowel and bladder alterations, and vascular connective tissue reactions. It must be remembered that late complications may occur.—*A. W. Sommer, M.D.*

Fried, Carl. Die Röntgentherapie der Knochenmetastasen nach Mammacarcinom. Ihre unmittelbaren Wirkungen und ihr Einfluss auf die Prognose. (Roentgen therapy of bone metastases from mammary carcinoma; its immediate effects and its influence on the prognosis.) *Radiol. clin.*, May, 1950, *19*, 129–158.

After a brief review of the various auxiliary measures (administration of calcium and vitamin D, hormonal therapy, roentgen sterilization, etc.), the author discusses in considerable detail the incidence, time of appearance, clinical course and roentgen therapeutic response of bone metastases from primary carcinoma of the breast. His series includes 37 cases which were treated at the Instituto do Radium, São Francisco de Assis, São Paulo, Brasil.

The following pertinent data were obtained: incidence, 19.5 per cent; age distribution, 59.2 per cent between forty and sixty years; time of appearance, 43.3 per cent during the first, 24.5 per cent during the second, and 21.7 per cent during the third year after operation; time of appearance in relation to age, eleven months between thirty and forty years, sixteen months between forty and fifty years and 26.1 months in women over fifty years of age; frequency of bones involved in decreasing order, pelvis, femora, cervical spine, lumbosacral region, thoracic spine, ribs, pubic bone, skull and humerus.

The roentgen therapy was carried out with 180 kv., 1 mm. Cu and later with 200 kv., 2 mm. Cu, this latter giving a half-value layer of 2.12 mm. Cu. The technique is described at length. In general, large doses were used amounting to 3,000–5,000 r in single

foci or regions and 15,000–20,000 r in multiple metastases.

Of the 37 patients treated, 23 died, 7 could not be traced and 7 are still alive. The average survival after the first treatment was 13.3 months as compared with 4.7–5.1 months in the untreated cases. In the entire group 15 patients lived more than one year. Of those who died, 8 survived for periods between one and two years eight months; in the 7 still living the survival varies between one year and five years three months, the average being two years eight months.

In concluding, the author expresses the opinion that direct intensive roentgen irradiation constitutes the method of choice in the treatment of bone metastases from primary carcinoma of the breast. The other auxiliary methods mentioned above have only partial or temporary influence.—*T. Leucutia, M.D.*

RADIOISOTOPES

Doniach, I., and Pelc, S. R. Autographs with radio-active iodine. *Proc. Roy. Soc. Med.*, Dec., 1949, *62*, 957–959.

The authors refer to a previous publication for the detailed description of their technique for the preparation of autoradiographs. The final preparation consists of a 5 μ section of thyroid mounted on a glass slide and covered by a closely attached strip of developed photographic emulsion 2–3 μ thick. Concentrations of blackened photographic grains indicate the presence of radioactive material in the underlying tissue. The slide may be viewed unstained, or the sections may be stained before applying the film or after photographic processing.

Experimentation with rats sacrificed at varying time intervals showed I^{131} uptake in the follicular colloid within ten minutes after subcutaneous or intraperitoneal injection. In $2\frac{1}{2}$ hours there was greatly increased I^{131} uptake and, though all follicles contained I^{131}, concentration was greater in the center than in the periphery of the gland. By forty-eight hours I^{131} had disappeared from many central follicles though it was still present in the peripheral ones. This rapid turnover centrally was confirmed in autoradiographs made after four, seven and nine days. No autoradiographs were obtained when the rats were given thiouracil before or with the I^{131}.

The principal subject of this study was the rat thyroid gland; however, a few autoradiographs of human thyroids were made. They were successful provided the patient had had no previous iodine therapy. Administration of 20–100 microcuries of I^{131} by mouth 24–48 hours before thyroidectomy proved adequate.—*D. R. Bernhardt, M.D.*

Myant, N. B., and Pochin, E. E. The thyroid clearance rate of plasma iodine as a measure of thyroid activity. *Proc. Roy. Soc. Med.*, Dec., 1949, *62*, 959–961.

The quantitative measurement of I^{131} present in the thyroid gland, plasma and urine following an oral or intravenous dose of I^{131} is presented as a method of study of the thyroid gland.

Doses of 30 microcuries of I^{131} have been used, either with no carrier or with 20 micrograms of inert iodine. Euthyroid subjects continued to take up I^{131} for two to three days reaching a peak of about 33 per cent of the dose. The I^{131} content then started to fall slowly. In a group of untreated thyrotoxic patients the maximum uptake was greater, was reached earlier, and the I^{131} was lost more rapidly in the ensuing days. In each group the urinary rates correspond, an initial stage of rapid excretion being complete in about two days in normal subjects when 60 per cent of the dose has been excreted, excretion continuing at a slower rate thereafter. In thyrotoxics the initial stage is completed earlier, accounts for a much smaller percentage of the dose, and is followed by a faster rate of subsequent excretion. The plasma concentration of I^{131} reflects the same time scale. In normal subjects it falls to a low value in two days, during which time the activity is due to iodide. The concentration then rises again slowly, the activity now being due to organically bound I^{131} (thyroxine). After administration of the dose the thyroxine fraction has been detected in two days but not before. In thyrotoxics the iodide fall is more rapid and the thyroxine rise occurs earlier and is greater. The radiothyroxine is commonly present by seven hours.

After one or two hours following the oral dose the tissues have a normal iodide concentration. The I^{131} present in the plasma at this time exists only in the iodide state, not yet being elaborated as radiothyroxine. It is therefore possible to determine the rate at which the thyroid gland clears I^{131} (as iodide) from the plasma. In normal subjects the thyroid clearance rate is 5–40 ml. of plasma per minute; 15 thyrotoxic patients all showed more than 100 ml./min. The clearance in myxedema has been only a few ml./min. The values observed in non-toxic goiter have been normal or slightly elevated. The renal clearance for iodide has averaged 30 ml./min. and is unchanged in thyrotoxicosis.

For good results these tests must be done carefully and with understanding. This more complex method of determining thyroid clearance rate seems, likely to be of value in the more precise analysis of thyroid physiology and disease.—*D. R. Bernhardt, M.D.*

Mason, A. Stuart. Urinary excretion of radioactive iodine as a measure of thyroid activity. *Proc. Roy. Soc. Med.*, Dec., 1949, *62*, 961–962.

A group of 49 patients with clinical evidence of euthyroidism, hypothyroidism, and hyperthyroidism was studied to determine the value of urinary excretion of I^{131} as a measure of thyroid activity. Ten

microcuries of I^{131} with carrier were given orally. In twenty-four hours 26 normal subjects excreted 28–72 per cent of the dose. Nineteen cases of thyrotoxicosis showed 5–26 per cent excretion. Four cases of myxedema showed values in the normal range. During the first six hours following the tracer dose the excretion of I^{131} was not markedly different in the three groups. The subsequent period from six to twenty-four hours showed an obvious difference. In this period the excretion by normals varied from 10–25 per cent while the highest amount excreted by the mildest case of thyrotoxicosis was 4.5 per cent. In myxedema the values lay between 26 and 33 per cent.

The sources of error using the urinary excretion of I^{131} as a measure of thyroid function are renal insufficiency and previous administration of iodine.

This test is a simple useful diagnostic aid in determining thyroid activity. Urinary samples from six to twenty-four hours after administration of the dose give a clear-cut separation between the normal and the thyrotoxic subject. The test does not quantitate the degree of hyperfunction.—*D. R. Bernhardt, M.D.*

Fraser, Russell, Miller, H., and Reiss, Max. Clinical use of radio-active iodine. *Proc. Roy. Soc. Med.*, Dec., 1949, *62*, 962–968.

Dr. Russell Fraser: The use of I^{131} for the study of thyroid dysfunction and as a tracer substance in tumor detection is discussed.

The dosage used in the patients upon which this paper was based was 10 μc. of I^{131}. This delivers about 30 r to the normal thyroid. Examination of urine specimens collected for forty-eight hours show complete and reliable separation of typical cases of thyrotoxicosis and myxedema. The adequacy of the urinary collection can be checked by concurrent creatinine estimations and by assessing the uniformity of the excretion trend in the samples. The mean excretion at eight to twelve hours of the thyrotoxic group is one-tenth that of the normal control group. The obvious myxedema cases showed five times the normal excretion between twenty-four and forty-eight hours following the test dose.

No abnormal results were obtained in patients without evidence of thyroid disease when cases of renal failure with uremia were excluded. Patients with thyroid enlargement without clinical evidence of dysfunction gave normal results as a group. Primary and secondary thyroid malignancy showed no abnormality. One case of acute thyroiditis indicated hypothyroidism by this test, but there was no evidence of lack of circulating hormone. Three of 5 non-toxic goiters gave normal results. One of the 2 patients with non-toxic goiter who gave abnormal findings was pregnant. Subsequent observations on pregnant women suggest that pregnancy alone does not explain the low value obtained.

The presence of a normal function or hyperfunction of the thyroid gland, as indicated by the measurement of the urinary excretion of I^{131}, corresponded well with the final evaluation of the thyroid status in a series of cases clinically suggesting thyrotoxicosis.

Dr. H. Miller: A study of patients with normal thyroid function showed an average of 47 per cent of the tracer dose to be in the thyroid gland in twenty-four hours. The percentage excreted in the urine in twenty-four hours averaged 42 per cent. Patients with toxic goiter showed 69 per cent in the gland and 12 per cent excreted in the urine in twenty-four hours.

The thyrotoxic subject shows a rapid decrease in radioactivity of the blood following administration of I^{131}. This is due to the rapid removal of I^{131} from the blood by the thyroid gland. A secondary increase in activity of the blood is due to the excretion of active iodine by the thyroid gland. The euthyroid patient shows a steady fall in blood activity following administration of I^{131}. No secondary peak is seen in normal cases.

Dr. Max Reiss: It has been found in the human that thyrotrophic hormone increases the avidity of the thyroid for I^{131} and decreases the excretion rate. The different reactions of hypotrophic patients to treatment with thyrotrophic hormone can be used for differentiation between primary (thyrogenous) and secondary (hypopituitary or cerebral) hypothyrotic cases.—*D. R. Bernhardt, M.D.*

Miller, William B., Jr. Use of a wire recorder for recording Geiger-Müller pulses. *Science*, June, 9, 1950, *111*, 626–627.

Medical research and clinical studies with radioisotopes often require measurements to be made in many locations. This necessitates a large number of scalers and counters, which in turn creates a financial burden.

A Geiger-Müller tube with power supply and a commercial wire recorder solves the problem nicely. After the recording is made, it is played back through a Geiger-Müller counter amplifier, pulse shaping circuit and scalar. The end result is exactly like that obtained by using the Geiger-Müller counter directly.

Other advantages of the wire recorder are that it can be replayed if a check is desired. It is possible to record simultaneously on the same wire counts from two separate Geiger-Müller tubes.—*R. A. Hays, M.D.*

Patton, Henry S., and Millar, R. Gordon. Accidental skin ulcerations, from radioisotopes; recognition, prevention and treatment. *J.A.M.A.*, June 10, 1950, *143*, 554–555.

The danger of skin ulcerations from radioisotopes is advanced. The case of a patient with chronic lymphatic leukemia in whom a small amount of

yttrium 90 was accidentally deposited beneath the skin of the arm during intravenous injection is presented. An ulcer developed twenty-one days after the treatment, which refused to heal. Finally wide excision and skin graft were performed and a good take obtained.

It is recommended that isotopes given intravenously be administered via the intravenous drip method and that this be running some time before the radioactive material is introduced.—*R. A. Hays, M.D.*

Jaffe, Henry L., and Ottoman, Richard E. Evaluation of radioiodine test for thyroid function. *J.A.M.A.*, June 10, 1950, *143*, 515–519.

The authors studied 152 cases suspected of having some alteration of thyroid function. The physiology of the thyroid in relation to iodine retention is discussed. The history of the development and progress in the use of I^{131} in the investigation of thyroid physiology is reviewed.

In their hands, tracer studies with I^{131} were very accurate in the diagnosis of thyroid dysfunction. They had 95 per cent accuracy as compared to 67 per cent accuracy for the basal metabolism and 80 per cent accuracy for the protein bound blood iodine test.

Their tracer studies are carried out using 100 microcuries of I^{131} in 10 cc. of distilled water by mouth. The uptake is measured in twenty-four hours with the Geiger-Müller tube fixed at 10 cm. from the thyroid. They considered anything under 15 per cent as low and over 35 per cent as high. The authors admit the value of urinary excretion of I^{131} in the diagnostic work-up of thyroid cases but purposely did not report on it in this paper.

The advantages of this method of study are its ease to the patient and its consistent accuracy.—*R. A. Hays, M.D.*

Blumgart, Herrman L., Freedberg, A. Stone, and Kurland, George S. Hypothyroidism produced by radioactive iodine (I^{131}) in the treatment of euthyroid patients with angina pectoris and congestive heart failure; early results in various types of cardiovascular diseases and associated pathologic states. *Circulation*, May, 1950, *1*, 1105–1141.

Hypothyroidism, induced by radioactive iodine (I^{131}) to lessen the work of the heart, is proposed as a means of treating euthyroid patients with angina pectoris and congestive heart failure who are refractory to the standard medical measures. The writers give their results in various types of cardiovascular diseases. The author's excellent summary and conclusions are reproduced in their entirety.

1. The therapeutic results of hypothyroidism induced by radioactive iodine in 18 euthyroid patients with intractable advanced angina pectoris or congestive heart failure are reported. The duration of post-treatment observation was seven to twenty-four months and averaged thirteen months.

2. Persistent hypothyroidism can be regularly induced by one or more appropriate doses of radioactive iodine (I^{131}).

3. No radiation sickness and no toxic effects on the blood or kidneys have been observed. Mild or moderate transitory thyroiditis occurred in 10 patients, was severe in only 1 and was absent in 7. Temporary mild hyperthyroidism occurred in 2 patients.

4. Each patient received orally a total of 25.5 to 150 millicuries in single or divided doses, of which a total of 7.3 to 39 millicuries was retained within the body during the following seventy-two hours. The largest single dose was 56 millicuries.

5. The average total dose was 54.4 millicuries; the average three day retention, 17.9 millicuries.

6. Only patients were treated who were seriously incapacitated despite all standard forms of therapy and marked restriction of activities for many months or years.

7. Angina pectoris has been strikingly lessened or abolished in 8 of the 13 patients with intractable cardiac pain. Several patients have been rehabilitated and are gainfully employed. Concomitant congestive failure present in several of these patients was likewise improved. In the other 5 of the 13 patients, angina pectoris was greatly relieved when the patients were myxedematous but recurred when thyroid was administered to ameliorate the discomfort of myxedema.

8. Three of 5 patients incapacitated primarily because of congestive heart failure have shown worthwhile improvement; in 2 of these the improvement has been striking.

9. Tentative criteria for the selection of patients are presented, and the pre- and post-treatment management of the clinical course is described.

10. In the clinical management of these patients the authors have attempted to maintain the lowest metabolic rate consistent with the comfort of the patient and have administered small doses of thyroid after the induction of myxedema.

11. This group represents the intractable cardiac cripples who are ordinarily considered for surgery. Hypothyroidism induced by radioactive iodine promises to accomplish worthwhile improvement through medical means without the inevitable risk and complications of surgical intervention.

12. This procedure is therefore proposed as a means of treating angina pectoris and congestive failure refractory to the standard medical measures and is submitted for further investigation by other workers in this field.

13. Final evaluation of this therapy must await prolonged study. At present it can be said that many months of worthwhile existence already have been added to the lives of these disabled cardiac

patients who were refractory to all standard forms of medical therapy.—*R. F. Niehaus, M.D.*

Kreutzer, F. L., Miller, E. R., Soley, M. H., and Lindsay, S. Histologic localization of absorbed radioactive iodine in some human thyroid diseases. *Arch. Surg.*, April, 1950, *60*, 707–720.

An oral tracer dose of 250 microcuries of I^{131} was administered to 35 patients with various thyroid diseases to determine the localization of the iodine in the thyroid tissue. Measurements over the gland were made 24 hours later and following this the thyroid was extirpated. Radioautographs were made from the histologic sections of the gland.

In general, it was found that radioactive iodine is taken up in the acinar epithelium and is stored in the colloid. Patients with nodular glands took up radioactive iodine in direct proportion to the degree of hyperplasia present in the nodule. Two cases of adenoma demonstrated no uptake in the adenomatous tissue while the surrounding normal thyroid showed a good uptake. Diffuse toxic goiter showed a good uptake evenly distributed throughout the gland. Preoperative preparation with strong iodine will saturate the gland and the uptake will be low for I^{131}.

Thyroiditis exhibited an uptake of 9 per cent of the administered radioactive iodine. The areas of lymphocytic infiltration and disorganized acinar structure had no demonstrable uptake.

Fifteen cases of thyroid cancer were studied. Although the average total uptake of the extirpated gland was 20 per cent, it was confined to the normal non-invaded thyroid. Only one of the 15 cases of carcinoma took up a significant percentage of the I^{131}. Sections from this case revealed that there was good acinar structure and the uptake was due to functioning cancerous tissue.

The authors conclude that radioactive iodine can be of only limited usefulness in the treatment of cancer of the thyroid. Preliminary treatment with thyrotropic hormone or complete thyroidectomy may result in a greater percentage uptake in surgically inaccessible metastases.—*R. A. Hays, M.D.*

Gross, J., Leblond, C. P., Franklin, A. E., and Quastel, J. H. Presence of iodinated amino acids in unhydrolyzed thyroid and plasma. *Science*, June, 2, 1950, *111*, 605–608.

Iodinated amino acids in unhydrolyzed thyroid and plasma were studied in albino rats, using tracer doses of I^{131} and paper chromatography. Control studies were done using carriers of thyroxine, diiodothyromine, diiodotyrosine and monoiodotyrosine.

Chromatography of n-butanol extracts of the thyroid tissue and plasma were performed. After development in two dimensions, the filter paper was placed against roentgen film and a radioautograph was obtained. The filter paper was then painted with ninhydrin to color the carrier amino acids and compared with the radioautographs.

Plasma from the radioiodide-treated rats and controls was handled in a similar manner.

The results showed that the thyroid gland contained small amounts of monoiodotyrosine, diiodotyrosine and thyroxine besides thyroglobulin and iodide, as previously suggested by De Robertis. Thyroxine was found to be the only thyroid constituent in the plasma. The failure to find significant amounts of the other iodinated amino acids in the plasma is explained by their destruction within the follicle and a reutilization of their iodine. The thyroxine in the plasma is found combined with protein. The nature of the complex is not completely known.—*H. L. Friedell, M.D.*

Roswit, Bernard, Sorrentino, J., and Yalow, Rosalyn. The use of radio-active phosphorus (P^{32}) in the diagnosis of testicular tumors; preliminary report. *J. Urol.*, April, 1950, *63*, 724–728.

It has been experimentally established that tumor tissue and rapidly multiplying normal tissue cells have a higher and more rapid uptake of phosphorus than normal cells. The authors utilize this fact in the diagnosis of malignant testicular tumors. They administered P^{32} orally to 6 patients with testicular tumors who were operated upon later. A differential uptake of 25 per cent was accepted as the normal upper limit. Greater uptake than 25 per cent was considered as suggestive of malignancy. By means of this study it was possible to make the correct diagnosis in 4 of 6 cases of testicular tumor which were eventually operated upon.

One patient had a false negative test and 1 a false positive. The reasons for failure of the test are discussed in detail. The authors feel the preliminary investigation done here suggests that this test may have future diagnostic value in testicular tumors.—*R. M. Harvey, M.D.*

Nardi, George L. Localization of C^{14} in the tissues of mice after administration of C^{14} methyl-labeled glycine. *Science*, April 7, 1950, *111*, 362–363.

Carbon labeled compounds offer a wide range of experimental possibilities to both the biochemist and clinician. However, C^{14} has a very long half-life (5,200 years), and this fact has retarded its use because of the dangers of exposing tissues to the action of beta rays for long periods of time.

Some investigators have found that C^{14} as $BaCo_3$ or $NaHCo_3$ tends to localize in bone and remain there long after the soft tissues were no longer active.

The authors undertook further study on the use of a soluble compound. Glycine labeled with C^{14} in the methylene position was injected into mice and

the animals were sacrificed at intervals from six hours to forty-three days. C^{14} in this compound was evenly distributed throughout the tissues of the body. The specific activity of bone was not greater than that of the soft tissues. The total activity of each tissue showed a steady drop over a period of time so that after forty-three days only 5.54 per cent of the total injected dose was present in the body. Eight to 70 per cent is lost as radioactive CO_2 in the breath in the first forty-eight hours; thenceforth there is a slow but steady loss in the urine, feces and breath.—*R. A. Hays, M.D.*

Hahn, P. F., Haas, Victor H., and Wilcox, Aimee. Arrest of development of Plasmodium gallinaceum in mosquitoes (Aedes aegypti) by radiation effect of P^{32}. *Science*, June 16, 1950, *111*, 657–658.

Mosquitoes were permitted to engorge on chicks infected with avian malaria parasites, *Plasmodium gallinaceum*. Thereafter the mosquitoes were provided daily with 5 per cent glucose solution containing radioactive sodium phosphate. Other mosquitoes similarly infected were provided with glucose solution only.

After nine days, the stomachs of some of the mosquitoes of each group were examined. No difference in the average numbers or stage of development of oöcysts was noted. Five days later the salivary glands were dissected and no sporozoites were found in mosquitoes given P^{32}. Most of those given glucose alone showed the sporozoites.

Measurements of the radioactivity of the salivary glands demonstrated an average of 2,400 cpm. No deleterious effects were apparent in the mosquitoes themselves during the period of observation.—*R. A. Hays, M.D.*

Pochin, E. E. Investigation of thyroid function and disease with radioactive iodine. Part I. *Lancet*, July 8, 1950, *2*, 41–46.

In estimating the simultaneous thyroid uptake, plasma concentration and urinary excretion of radioactive iodine at hourly intervals for a period of six hours, several interesting observations can be made in euthyroid and hyperthyroid patients. If the urine content and the thyroid content of radioiodine are determined, the so called extrathyroid tissue content can be estimated by subtracting the sum of the two determinations from the total dose of I^{131} given. If the total extrathyroid content is compared with the plasma concentration per liter, the radioiodide space can be calculated. At the end of two hours a limiting value of 25 liters or 40 per cent of the body weight was found in the average euthyroid patient. In the case of hyperthyroid patients, the radioiodide space was found to be greater than normal at the end of one hour. This radioiodide space is not a true measure of anatomical volume since it is known that saliva and gastric juice have many more times the concentration of I^{131} than does plasma.

When the actual rates of removal of I^{131} by the kidney and thyroid were studied, these rates were found to be proportional to the concentration of I^{131} in plasma at the time. If the renal excretion rate is plotted against plasma concentration, the two are found to be directly proportional to each other. The hourly excretion of I^{131} equalled that amount of iodine which could be cleared from approximately 2 liters of plasma—that is, if the kidney excreted 8 per cent of the dose per hour, the plasma was found to contain 4 per cent of the dose per liter. The values varied widely with an average of 32 ml. per minute with a standard deviation of 12 ml. per minute.

Thyroid clearance rates could be similarly determined by direct measurements of the thyroid gland and measurements of I^{131} plasma content per liter. The thyroid clearance rates were found to vary from 7 to 42 ml. per minute with an average of 25 ± 8 ml. per minute in normal subjects. In Graves' disease the values ranged from 85 to 500 ml. per minute, with an average of 240 ml. In myxedema, the clearance rates ranged from 1 to 4 ml. per minute.

The author states that it is not anticipated that any of these studies will rigidly separate normal from hyperthyroid and hypothyroid states since there is such a wide variation in normals, but it is his impression that the differentiation will be sharper in this fashion than other methods utilizing I^{131} uptake or excretion.

The pitfalls of using twenty-four hour total urine excretions and thyroid uptake studies as criteria for Graves' disease are discussed. The author suggests a simple test, utilizing the ratio of counts over the thyroid to total counts over the thigh, measured at one hour. He has demonstrated that this is closely related to thyroid clearance rates. In the cases presented it has proved very satisfactory. This involves simple measurements and requires no blood or urine samples.—*H. L. Friedell, M.D.*

Pochin, E. E. Investigation of thyroid function and disease with radioactive iodine. Concluded. *Lancet*, July 15, 1950, *2*, 86–91.

The first phase of the iodine cycle (thyroid uptake of iodide) was reported in the author's first report of this series (see above abstract).

The second phase deals with the retention of iodide by the thyroid gland. In normal subjects after the first three days the total radioiodine content of the gland falls by only a small percentage (approximately 0.6 per cent of the dose per day). Since there is a continuing thyroid uptake of 0.3 per cent per day, the loss of the gland iodine is therefore 0.9 per cent of the dose per day. In hyperthyroidism the radioiodine content decreases by six per cent of the dose per day despite a high continuing daily intake of 8 per cent. The daily output by the gland must therefore be 14 per cent of the dose. Iodine uptake

cannot be determined directly but is estimated by making an assumption that the ratio of kidney excretion rate and thyroid uptake rate are directly related. (The author indicates why these assumptions appear valid, but feels that further work is needed to justify calculation of the thyroid intake from urinary output.) Based on such assumptions, the mean stay of the radioiodine atom in the gland has been calculated in 12 patients with Graves' disease and was found to be approximately five days. In 8 normal patients the mean stay was found to be approximately five weeks. It seems clear that the time spent by iodine atoms in their passage through the thyroid gland in Graves' disease is greatly reduced and the acceleration of thyroid iodine turnover may prove to closely parallel the rapidity of iodide uptake.

Studies on radioactive thyroxine show that it is first detected in the plasma within three to seven hours after a given dose in hyperthyroid patients. The thyroxine level was found to rise exponentially toward a plateau with the latter level being maintained for several days. The mean lifetime of thyroxine in the plasma was found to be two days in Graves' disease.

The remainder of the article deals with localization of radioiodine in various tissues. In Graves' disease there was selective localization over the liver, the radioactivity presumably being radiothyroxine.

A case of a functioning carcinoma of the thyroid with metastases treated with I^{131} is reported. Considerable improvement in the patient's general condition as well as a decrease in size of the metastatic disease was observed.—*H. L. Friedell, M.D.*

Gordon, Edgar S., and Albright, Edwin C. Treatment of thyrotoxicosis with radioactive iodine. *J.A.M.A.*, July 29, 1950, *143*, 1129–1132.

The treatment of 120 patients with radioactive iodine is discussed; 86 of the patients were females and 34 were males; 83 cases had a diffuse goiter and 37 were of the nodular variety; 22 patients had had previous thyroidectomies. The conventional dosage determination by means of thyroid retention of a tracer dose and size of the gland was used. The authors failed to report the dose necessary to produce remissions in microcuries of radioiodine per gram of gland. They recognize, however, the difficulties which are entailed in such an estimate and the marked variation in these dosage estimates as reported by others. They emphasize also the individual differences in radiosensivity which increases the uncertainty of such dosage estimates.

The multiple dose method was used in treating the patients. Under this regimen, 59, or 49.1 per cent, of the patients were controlled by one dose with an average dose of 3 mc.; 36 patients required two doses with an average total dose of 5.1 mc.; 16 patients required three doses with an average total dose of 6.29 mc.; 7 patients required four doses with an average total dose of 10 mc.

Of the 120 patients treated, 5 were lost from follow-up and 3 died of other causes. Three patients (2.5 per cent) developed hypothyroidism, although the doses of I^{131} received were not greater than 3.5 mc. in any case. The results in the remainder of the cases were excellent.

No difference in sensitivity to I^{131} could be detected in diffuse or nodular goiter. No untoward reactions were noted. The clinical problems involving radioiodine therapy are discussed, including dosage and variation in sensitivity to radiation. The use of I^{131} is considered the treatment of choice where no mechanical difficulties from the size of the thyroid exist.—*H. L. Friedell, M.D.*

Perry, W. F., and Gemmell, J. P. The use of radioactive iodine in the diagnosis of hyper- and hypo-thyroidism. *Canad. M. A. J.*, May, 1950, *62*, 484–490.

The authors question the relative reliability of methods utilizing radioiodine and plasma-protein-bound iodine determinations in the diagnosis of thyroid disorders. With this problem in mind, they undertook a study of the relative merits of both methods.

It was found that measurements combining the sharpest differentiation with the greatest simplicity were the determination of the twenty-four hour thyroid uptake of radioactive iodine and the estimation of the amount of the isotope excreted in the urine in the period between fifteen and twenty-four hours after administration. The concentration of radioactive protein-bound plasma iodine was greater at all times in hyperthyroid subjects examined; however, those with hypothyroidism had concentrations comparable to the euthyroid subjects examined.—*Moris Horwitz, M.D.*

Bélanger, Leonard-F. A method for routine detection of radiophosphates and other radioactive compounds in tissues; the inverted autograph. *Anat. Rec.*, June, 1950, *107*, 149–159.

The usual method of radioautography consists in keeping the microscopic section and photographic emulsion in close contact throughout exposure, development, and mounting in such a way that the stained microscopic section and developed emulsion can be visualized together on a microscopic slide.

The two variations of this method have drawbacks, however. The "coated autograph" method, wherein the tissue section is stained and then covered with photographic emulsion, results in loss of phosphates from the tissue sections. In studies of bone with P^{32}, this changes the exposure of the emulsion. Evans' "mounted autograph" technique, in which the histologic sections are placed directly on the

emulsion surface of a photographic plate, results in changes in the histologic section during its passage through the photographic developer and fixer. Also, uneven and spotty development is common and stain is taken up by the emulsion.

A new method of radioautography is described which permits easy operation under a relatively bright filter. Postautographic staining is done which allows retention of all the P^{32} for autographic purposes and with inversion of the mounted specimen, easier and better staining is possible. One disadvantage is loss of resolution of the areas containing the radioactive material when they are not widely separated in magnification of less than 100 diameters. —*Robert Emerick, M.D.*

CHEMOTHERAPY

Huguenin, R., Hébrard, and Saracino, R. Disparition d'un vaste épithélioma—développé sur radiodermite—sous l'influence de la chimiothérapie. (Disappearance of a large epithelioma—outgrowth of a radiodermatitis—under the influence of chemotherapy.) *Bull. Assoc. franç. l'étude cancer*, 1950, *37*, 168–175.

The authors report a spectacular regression and complete disappearance of a large epithelioma under the influence of two chemical derivatives of nitrogen mustard. The epithelioma (malpighian, basal cell type) developed on the scar of an old radiodermatitis of the scalp (roentgen epilation 26 years ago) which was secondarily traumatized (and ulcerated) two years ago. In 1949 the lesion was so proliferative and extensive that no other therapy was possible except to use nitrogen mustard derivatives.

They first tried triethanolamine (product of total hydrolysis of nitrogen mustard) but did not get any results. They used another derivative but again had no success. However, when they used β, β', β'' trichlorethylamine the lesion began to regress spectacularly. Of this 9 mg. was given in 8 intravenous injections at five day intervals. After six weeks they noticed that the lesion was ulcerating again. Then they used another derivative, the sulphide of β, β', β'' dichlorethyl of which they gave 6.5 mg. in 7 intravenous injections. The ulceration closed itself. A firm and almost complete scar developed. The adenopathy disappeared.

The irregularity of the action of the nitrogen mustard derivatives is thus evident. It remains to be seen whether or not this apparent healing will be a permanent one.—*J. N. Sarian, M.D.*

Frieden, Julian, and White, Abraham. Studies of electrophoretic serum protein patterns in subjects treated with pituitary-adrenal cortical hormones, nitrogen mustard, or x-radiation. *Yale J. Biol. & Med.*, May, 1950, *22*, 395–406.

Adrenal cortical secretion, regulated by the pituitary adrenotropic hormone, is a normally existing mechanism which produces lymphoid tissue involution. When this mechanism is augmented by the administration of adrenal cortical extract, there results a profound absolute lymphocytopenia due to the dissolution of lymphocytes. This is accompanied by a rise of antibody titer in the blood, occasioned by the release of a protein identical with serum beta and gamma globulin, which is contained in the lymphocytes.

This study seeks to investigate further the possible contribution of the lymphocyte to the production of serum beta and gamma globulin, by the administering of adrenal cortical extract, roentgen irradiation, and nitrogen mustard—all of which produce lymphoid involution—to human and animal subjects. The serum protein fractions of the subjects studied were divided into albumin, alpha$_1$ globulin, alpha$_2$ globulin, beta globulin, and gamma globulin. The Tiselius apparatus was used to measure the fractions by electrophoretic means.

In subjects who received adrenal cortical extract or roentgen irradiation, there were no consistent striking alterations in the serum protein pattern, even though there was a concomitant lymphocytopenia in many instances. Five patients were given nitrogen mustard; 3 of these showed a trend toward decrease of the beta gamma globulin fractions, which was not well correlated with the lymphocytopenia.

In explaining the lack of correlation between the serum globulin and lymphocyte count, the authors point out that roentgen rays and nitrogen mustard not only produce lymphocyte dissolution in the lymph nodes, but damage lymphocyte production also. Moreover, roentgen irradiation and nitrogen mustard therapy depress antibody globulin production. Other factors such as the state of nutrition of the subject, endocrine secretions, hemodilution, and the sensitivity of the measuring apparatus also play a part which must be more clearly evaluated.

Therefore, "unequivocal interpretation of data derived from studies of the type presented here is not possible."—*Gabriel Whiteman, M.D.*

Silverman, Frederic N. Treatment of leukemia and allied disorder with folic acid antagonists; effect of aminopterin on skeletal lesions. *Radiology*, May, 1950, *54*, 665–678.

The experimental studies of folic acid conjugates and the clinical employment of two conjugates, teropterin and diopterin, by Faber is described. The general attitude at this time is that there is no rationale for the use of folic acid conjugates in the treatment of malignant disease.

Folic acid antagonists were next used. Aminopterin has been the one most widely used. Faber and Dameshek have reported improvement clinically and hematologically along with prolongation of life in

30–50 per cent of children with acute leukemia. No permanent cure has been effected. Toxic manifestations are sometimes distressing but these disappear upon withdrawal of the drug.

Roentgen observations of skeletal lesions were made in a small group of children with leukemia, treated with aminopterin. Initial lesions, particularly transverse bands of diminished density at end of shaft of femur, regressed during the course of treatment, and new lesions appeared only terminally. Assessment of folic acid antagonists in the treatment of leukemia cannot yet be made. Observations of side-reactions may establish their value as experimental tools even if they are discarded for therapeutic use.—*E. E. Seedorf, M.D.*

Cohen, Lionel, and Kimmel, Samuel A. Treatment of simple epithelial cysts with secondary photoelectron radiation; preliminary report. *Brit. M. J.*, July 8, 1950, *2*, 87–88.

The use of heavy metal such as colloidal lead orthophosphate in the treatment of bone metastases has been reported in the literature. One factor in the beneficial effects of this compound is the increase during roentgen therapy of ionizing secondary electrons in the area where the lead is deposited.

The authors of this article have utilized another heavy element, bismuth, to produce intense local ionization sufficient to destroy the secreting lining membrane of a ranula.

Four cases of ranula are reported. Three of these failed to respond previously to either roentgen therapy or aspiration followed by injection of 2 ml. of 10 per cent aqueous suspension of bismuth oxychloride. However, when injection of the bismuth was followed by a tissue dose of approximately 300 r given at a single sitting, a complete cure was obtained within three weeks in all cases.—*Robert Emerick, M.D.*

Weder, Carman. Urethane in the treatment of multiple myeloma. *Canad. M. A. J.*, June, 1950, *62*, 589–590.

A case of multiple myeloma is presented which showed clinical, histopathological, biochemical and hematological improvement on urethane therapy after failure to arrest the disease with stilbamidine.

Roentgen therapy applied to the painful areas of bone destruction will give symptomatic relief but has no effect on the course of the disease.

The dosage of urethane was 2 gm. daily for one week, then increasing to 4 gm. daily for one month, then 1.5 gm. daily. There was an immediate drop in total protein, abnormal globulin and a rise in albumin. There has been only a six month follow-up. —*R. J. Reeves, M.D.*

MISCELLANEOUS

Roper, William H. Duplication of roentgenograms by artificial solarization; with emphasis on a simple standardized technique. *Am. Rev. Tuberc.*, May, 1950, *61*, 725–729.

Solarization is a term applied to a direct method of copying roentgen films. A contact copy is made by a long exposure to light, either solar or artificial. By using the correct exposure range, the copy will be the duplicate of the original; shorter and longer exposures give a reversal of the original; that is, a positive film rather than a negative as the original.

A very satisfactory method for making such copies is described in detail. A 500 watt reflector-type fotoflood bulb is set in an overhead socket at a distance of approximately 50 inches above the table top. Specific details concerning all parts of equipment are enumerated in the article. Since the films are extremely sensitive to artefacts and static marks under these conditions, directions for proper handling of films are given.

The original film should be cleaned carefully before using. Exposure times vary from 20 to 60 seconds, the lesser amount being used for lighter or softer films, and greater amounts for darker films.

Densitometer tests on films copied by this method show that the relative densities are reproduced with surprising accuracy.—*Lois Cowan Collins, M.D.*

Axen, O., and Lind, John. Table for routine angiocardiography; synchronous serial roentgenography in two planes at right angles. *J.A.M.A.*, June 10, 1950, *143*, 540–542.

The authors describe a special table for angiocardiography, permitting simultaneous exposures at right angles to each other. Ten exposures may be made in each direction in a period of from five to ten seconds. An electrocardiogram is made throughout the exposures to fix precisely the time between exposures as well as to register the heart phases in which the exposures have been made. The simultaneous projection in both the right and left oblique directions facilitates precise identification of the various chambers, and gives some concept of the dynamics of the heart. A better estimation of chamber capacity may be made.—*C. N. Borman, M.D.*

Pearl, Felix, Friedman, Meyer, Gray, Norman, and Friedman, Bruce. Coronary arteriography in the intact dog. *Circulation*, May, 1950, *1*, 1188–1192.

This article concisely and clearly describes a dependable and apparently safe method whereby the coronary arteries of dogs with intact chest can be demonstrated roentgenologically. The method consists of the injection of 4 cc. of 70 per cent diodrast solution through a special thin-walled, woven,

radiopaque catheter which is inserted into the carotid or femoral artery and passed to the proximal aorta or the left ventricle under fluoroscopic observation. Electrocardiograms taken during the procedure were normal. Clear cut, contrasting arteriograms are reproduced showing coronary arteries, separate cusps of the aortic valves, and the proximal aorta. (Four excellent roentgenologic reproductions are included.)

The writers believe that the development of a safe and dependable method for coronary arteriography has important implications in respect to the diagnosis and possible treatment of disturbances of the coronary circulation in man, and in experimental coronary artery disease in animals.—*R. F. Niehaus, M.D.*

Andervont, Howard B., and Dunn, Thelma B. Attempt to detect a mammary tumor-agent in strain C mice by x-radiation. *J. Nat. Cancer Inst.*, April, 1950, *10*, 1157–1189.

The authors report on another attempt to enhance the activity of the mammary tumor agent in strain C mice, or to lower the resistance of the mice to the agent, by the use of roentgen radiation.

A short review is first given concerning previous experiments to detect, if possible, the mammary tumor agent in strain C female mice.

Methods and materials were as follows: Laboratory raised animals were used. Those under observation for the appearance of mammary tumors were kept 8 to a cage, and were examined every other week for palpable tumors. Histologic sections were prepared from every tumor found.

Various procedures are discussed for detecting the presence of the mammary tumor agent in tumors and also in tumor-bearing mice.

The experiment was started by irradiating 25 litters of strain C female mice (low tumor strain females) with whole body roentgen radiation in doses of 25, 50, 100 or 200 r. Following this procedure, these mice were then bred with non-irradiated high-mammary tumor strain C_3H males. One mouse from each litter was kept as non-irradiated control. The ideal litter was 5 mice, 1 a control, the other mice given roentgen irradiation. Litter groups were of different ages; 15 litters were 1–4 days old, 10 litters 12–14 months old.

Detection of the agent in the 5 hybrids was accomplished by permitting them to suckle their litters. In some in which suckling was unsuccessful, inoculation technique was used.

Tumor incidences of 71 to 86 per cent in the hybrids born to non-irradiated mothers approximated results of previous experiments. Tumor data in hybrids born to irradiated C females were similar to those born to non-irradiated females. The only difference was the lower average age at which tumors occurred in the C females irradiated with 200 r.

The over-all results indicated that the procedure did not influence the activity of the agent. The incidence of mammary tumors in offspring of non-irradiated C females was the same as those derived from irradiated animals.

Studies on the histopathological appearance of the tumors in the hybrids revealed four groups. Three groups were forms of adenocarcinoma, the fourth group was adenocanthoma.

Type A adenocarcinomas predominated in the 5–19 month old hybrids, and were the only tumors encountered in 5 young agent-bearing hybrids. Type B predominated in hybrids over 19 months old. Thus there was a correlation in the morphology of these mammary tumors and the age of the animals in which they arose.—*L. Lemak, M.D.*

Douglas, D. M., Ghent, W. R., and Rowlands, S. Atrophy of the gastric glands produced by beta rays; histological findings in animals. *Lancet*, June 3, 1950, *1*, 1035–1038.

Since external roentgen irradiation over the stomach reduces gastric secretion, but has the disadvantage of simultaneously affecting liver and pancreas, the authors devised a method of selective local irradiation of the gastric mucosa, not effecting adjacent organs. A rubber balloon, painted with a latex solution containing 75 millicuries of P^{32}, was attached to a stomach tube. The balloon was then passed into the stomach of trained dogs, distended with barium emulsion to insure good contact, and left in position for five to nine hours.

The estimated average dose to the gastric mucosa was 5,000 r, with the first few millimeters of mucosa receiving 20,000 to 25,000 r, and with no irradiation beyond the P^{32} beta-ray penetration range of approximately 8 mm. Biopsy specimens taken thirty-nine to seventy-four days after P^{32} irradiation showed varying degrees of atrophy of tubular glands of the stomach, without significant change in the submucosa or muscularis. The authors suggest that, if the method can be shown to produce consistent hypochlorhydria, it might prove safe and useful in the non-surgical therapy of duodenal ulcer in man.—*H. P. Brean, M.D.*

Bacq, Z. M., Herve, A., Lecomte, J., and Fischer, P. Cyanide protection against x-irradiation. *Science*, April 7, 1950, *111*, 356–357.

The recent reports of cysteine protection against roentgen radiation and experiments which showed that the intraperitoneal injection of hydrogen peroxide in mice was a radiomimetic poison led the authors to study the protective influence in mice of cyanide.

It had been shown that the –SH groups disappear in the skin of guinea pigs after roentgen irradiation

and that cyanide reduces disulfide bands (—S—S—) to sulfhydryl groups (—SH).

Several groups of mice were exposed to roentgen rays. The animals receiving 0.1 mg. of NaCN just before irradiation showed 50 to 80 per cent survival. All of the controls died between the fourth and ninth day following an exposure to 500 roentgens. NaCN given immediately after exposure and sodium thiocyanate (NaSCN) did not protect but did delay death. It appears that it is the —CN anion which protects.

Several theories as to the biochemistry involved in this cyanide protection are proposed but all require further investigative study.—*R. A. Hays, M.D.*

Crawford, J. N. B. Medical aspects of the effects of atomic explosion. *Canad. M. A. J.*, June, 1950, *62*, 529–534.

This article discusses medical aspects of the effects of atomic explosion.

When an atomic bomb explodes, great quantities of energy are released in the form of heat, light, blast, and radioactivity. The effects are variable, depending upon whether the bomb explodes in air or under water. Effects of explosion discussed in this paper were observed in Japan immediately following VJ Day with effects on experimental animals taken into consideration.

An atomic explosion differs from an ordinary bomb blast in the extent of its range. It is like a violent, sudden gust of air that lasts for a brief but appreciable period. It is so strong that ordinary buildings will be destroyed within a distance of 1 mile from ground zero. A city situated on a flat plane would be harder hit than one protected by hills. Building construction limits the amount of damage, with reinforced concrete buildings more resistant than wooden houses. Beyond a certain height the distance of air zero to ground zero becomes so great that the effect of the bomb is lessened. Primary blast produces casualties but these are less than might be expected. Japanese medical observers on the spot could not find any persons with direct damage to internal organs. Necropsy of cases dying early showed no evidence of blast damage to the lungs. One report gave a total of 17 ruptured eardrums discovered at Hiroshima, and 22 at Nagasaki.

Secondary blast injuries or mechanical injuries are more important. These result from flying or falling glass, timbers, bricks and other débris. Injuries produced are fractures, concussions and lacerations.

When the bomb explodes, vast quantities of radiant energy are released. This covers the entire width of the spectrum including ultraviolet, visible and infrared radiation. These produce thermal injuries. Light colored clothing offers more protection than dark colored and thick clothing or multiple layers more than thin or single. Direct injury to the eye is uncommon. Transitory blindness lasting 5 minutes is common. Flash burns are profile burns affecting only that surface of the skin which is exposed to the ray. At a distance of 1 mile from center, the burns were preceded by intense erythema, followed by increase in pigmentation. Symptoms associated with burns show a fairly definite pattern. Close to the blast, both burns and blisters appeared in 5 minutes. At 1 mile from center burns appeared in 2 hours, blisters in 4 to 6 hours. At 1¼ miles burns appeared in 3 hours and blisters in 10 hours. Flame burns produced by atomic explosion are identical to those produced by other causes. Burns of one kind or another were responsible for 20 to 30 per cent of deaths in the Japanese bombings.

Radiation injuries accounted for an estimated 7 to 20 per cent of the deaths. These should not be minimized but it should be pointed out that in an air explosion of a bomb, radiation effects are less important than the effects of blast or burning. Primary radiation in the form of alpha and beta particles, slow and fast neutrons, roentgen and gamma rays is produced when the bomb explodes instantaneously. Radioactive materials taken into the body by ingestion or inhalation may be dangerous by damaging effect on bone marrow. Neutrons have great range and high power of penetration. They will travel 1,500 meters through air. Against neutrons, the half thickness of steel is between 3 and 12 inches; of concrete, earth, and wood, about 6 inches; of water, 6 inches. Neutrons will render radioactive many familiar elements, such as sodium or carbon, against which they impinge. Gamma rays also have a great range and a high degree of penetration. Against gamma radiation, the half thickness of materials commonly used in construction are 1 inch steel, 3 inches concrete, 4 inches wood and earth. Gamma rays will render many elements radioactive. Roentgen rays are similar in effect to gamma rays, but have a less degree of penetration.

Fission products produced by the explosion of an atomic bomb are carried upward in an atomic cloud by the heat that is produced. If settled out in a concentrated area they may render the contaminated area dangerous to inhabitants.

Secondary radioactivity may be produced principally by neutrons bombarding familiar materials. Combination of induced radioactivity together with fission products sufficiently concentrated in the area may render it dangerous to lives for a period depending upon the radioactive decay of the elements concerned. Secondary radioactivity from ground and normal structural materials will have decreased to below the dangerous level within 2 minutes of the instant of explosion.

Biological effects of ionizing radiation comprised harmful effects on tissues according to their sensitivity such as lymph tissue, bone marrow, lymphocytes, lymph nodes, Peyer's patches, leukocytes, epithelial cells of the gonads, salivary glands, skin

and mucous membranes, endothelial cells, blood vessels, peritoneum, connective tissue cells, muscle cells and nerve cells. Effects of atomic bomb explosion chiefly concern one with acute total body radiation.

The lethal dose of radiation is found within a radius of about 1½ miles from epicenter of explosion and a dangerous dose is found out 2 miles from the epicenter.

Clinical effects of radiation from atomic bomb explosion include epilation, common in persons surviving more than 2 weeks, vomiting, a common early symptom, in many cases within 30 minutes after exposure. Diarrhea is common within the first few days, in many cases sanguineous, due to ulceration of Peyer's patches. Ulceration of tongue, larynx, esophagus and intestines occurs early. In 3 to 4 months enteritis, usually of the large intestine, may be found. Pseudomembrane formation and ulceration produce a picture much like that of bacillary dysentery. Radiation effects are discernible in the testis as early as the fourth day and are profound in all fatal cases within 1,500 meters of the bomb. Amenorrhea is common for 3 to 4 months following bombing but is not permanent. The lymphoid and hematopoietic tissues undergo rapid necrosis. There is a decrease in the total lymphocyte count most marked within 24 to 72 hours, and a moderate granulocyte luekocytosis appearing in two peaks 12 to 24 hours after exposure and then a progressive decline for the next 6 days. In non-lethal cases about 15 to 17 days after exposure small but sustained increase in granulocytes occurs. Reduction of platelets and red blood cells appears more slowly and is not so uniformly observed. Hemorrhage is a very common finding not only in the skin but in internal organs. The platelet count is reduced, the bleeding time increased as much as 46 minutes.

Two groups comprise the course of radiation sickness. "Patients who die within 2 weeks of exposure" and "patients who die later than the second week or who survive severe symptoms." Clinical course of each is given.

The diagnosis of radiation sickness can be made by clinical examination of a patient. A superior method of diagnosis of radiation sickness would be some sort of physical instrument such as a pocket dosimeter or film badge, to detect indication of radiation exposure. If it is known how much radiation this patient received, the subsequent fate of the patient can be fairly accurately predicted and patients can be sorted out for treatment purposes.

Treatment of casualties resulting from atomic explosion are principally the treatment of effects resulting from blast and burn. The medical man will be faced with difficult decisions in selection of cases for whom treatment is hopeless in order that it may be available to those who can be helped. An individual who has received acute total body radiation in excess of 600 roentgens will die within 9 to 10 hours. No specific treatment for radiation sickness has been discovered but intense research is continuing and a true specific may yet be found. At the present time treatment should be directed to rest and good nursing in order to give the patient the best opportunity to recover, utilizing his own resources. Other treatment is symptomatic and supportive.—*J. H. Gilmore, M.D.*

Van Allen, Willard W. Protecting photofluorographic personnel from excessive radiation. *Pub. Health Rep.*, July 7, 1950, *65*, 865–868.

In photofluorography, radiation hazards are present to a considerably greater extent than in other roentgenographic diagnostic procedures. The Electronics Laboratory has undertaken two programs in an effort to find the most effective procedures for the protection of photofluorographic personnel.

The first is the monitoring of the amount of radiation actually received by its personnel each week. This is done by having each employee wear a dental film in a plastic case for one week. After five weeks of this procedure the majority of technicians succeeded in reducing their radiation damage to less than one-sixth the accepted limit of 300 milliroentgens per week.

The second program was the study of radiation fields surrounding photofluorographic installations used by Public Health Service teams. The field of secondary radiation surrounding a typical installation is shown by means of isodose curves. Study of these curves shows where radiation hazards exist and ways of avoiding excessive exposure.—*G. J. Culver, M.D.*

Gerrie, John, Kennedy, Fred, and Richardson, S. L. Beryllium granulomatosis. *Canad. M. A. J.*, June, 1950, *62*, 544–547.

This is another single case report of a skin granuloma secondary to a cut with a broken fluorescent bulb.

The authors quote Coakley, Shapiro and Robertson who described four types of cutaneous lesions: (1) contact dermatitis where beryllium dust comes in contact with the skin over a period of time; (2) ulcers from implantation of beryllium sulfate crystals in lacerations; (3) cutaneous lesions in patients with pulmonary granulomatosis; (4) subcutaneous granuloma in cuts from fluorescent lamps, the lesions appearing like sarcoidosis.

One case reported by Doane (*J. A. M. A.*, 1949, *139*, 1047) is quoted in which roentgen therapy was used unsuccessfully for beryllium granuloma.

The pulmonary lesions are very briefly noted and reference is made to Pascucci (*Radiology* 1948, *50*, 23) and Wilson (*Occupational Med.*, 1948, *5*, 690)

for a discussion of the roentgenological aspects.—*Martha E. Mottram, M.D.*

Burke, Desmond T. A stereoscopic viewing desk designed for limited space. *Radiology*, May, 1950, *54*, 750–751.

The author has combined a reading desk and stereoscope into a floor space of 21 by 76 inches. The stereo view box is mounted flush, centrally in the surface of the desk and a Chamberlain-Stanford stereoscope runs on a track mounted at the back of the desk and extending 1 foot beyond the edge of the desk so that the stereoscope may be rolled beyond the working area of the desk when not in use. Eight conventional illuminated panels mounted on the wall behind the desk are used for routine work. A self-explanatory photograph accompanies the article.—*M. B. Goodwin, M.D.*

Levene, George, and Perkins, Charles B. The value of laminagraphy in the difficult gallbladder problem. *Am. J. Digest. Dis.*, July, 1950, *17*, 240–242.

The authors point out the high degree of accuracy in roentgen diagnosis of gallbladder disease. This is particularly true in cases with positive findings, but does not hold true in cases found to be negative, one of the greatest difficulties being the inability to detect stones.

Numerous techniques for better visualization of gallstones have been suggested, but even these procedures often fail to give sufficient evidence to permit diagnosis more definite than "suspicious of stones." In such cases the authors have employed laminagraphy and 3 cases illustrating gratifying results are presented.

The technique is described in detail. The authors conclude that even though the method is more time-consuming, if employed early enough in the examination it may save hours of watchful waiting to see what happens to a suspicious shadow. They also urge that since laminagraphy offers a definite diagnosis where other roentgenographic procedures fail, it be employed more often.—*R. D. Moreton, M.D.*

Alexander, Gilbert H., and Alexander, Ralph E. The use of gastric mucin as a barium suspension medium; a preliminary report. *Radiology*, June, 1950, *54*, 875–877.

In the search for methods of making a barium sulfate suspension adhere better to the gastrointestinal mucosa, a mixture containing gastric mucin was investigated. For the stomach and small bowel, 2 grams of mucin are dissolved in 250 cc. of a mixture containing 125 grams of barium sulfate. Preliminary study showed it to give better small bowel films. No advantage was found in the study of the esophagus, stomach or colon except in the retrograde filling of the small bowel. This preliminary report does not mention double contrast studies.—*M. B. Goodwin, M.D.*

Rosenberg, Lee S., and Simpson, James R. A simple serialographic technic for cerebral angiography. *Radiology*, June, 1950, *54*, 869–874.

A simple technique for exposing four 8 by 10 inch films in instances of cerebral angiography is described. The four 8 by 10 inch cassettes are placed in a Bucky tray from which the centering device and clamps have been removed. A large lead sheet the width of the roentgenographic table and about 3 feet long is strapped to the top of the table. In this sheet a rectangular opening 8 by 9 inches is cut so that the patient's head may be placed over this opening. The technician rapidly moves the tray containing the four cassettes so each film is exposed separately during the injection of the opaque media.

A diagram accompanies the article so one may visualize the procedure.—*C. A. Stevenson, M.D.*

Szenes, T. Eine Methode der Distanzmessung mit Röntgendurchleuchtung. (A method of distance measurement with the aid of roentgenoscopy.) *Radiol. clin.*, May, 1950, *19*, 178–183.

The author states that the modern roentgenoscopic apparatus cannot be used for orthodiagraphy without auxiliary equipment owing to the fact fact that the fluoroscopic screen and the roentgen tube move together. To obviate this disadvantage, he devised a special method of examination which is described in the present article.

The method is as follows: The fluoroscopic screen is fixed at a distance from the focus of the roentgen tube which is twice as great as the distance of the wall of the vertical stand or of the top of the horizontal table from the focus. A small lead-sign is fastened to the standwall or the tabletop behind the organ to be examined. The central roentgen ray is directed first to one and then to the other border of the organ and in each position the projected shadow of the lead-sign is marked on the fluoroscopic screen. The distance between the two points is equal to twice the diameter of the examined organ so that one-half of the distance corresponds to the actual diameter of the organ.

The accuracy of the method has been verified in practice. The author found it especially useful in the measurement of the aortic diameter.—*T. Leucutia, M.D.*

Root, Joseph C., and Rayle, Albert A., Jr. A device for roentgen examination of the colon following colostomy. *Radiology*, May, 1950, *54*, 732–734.

A custom made suction device is described as an aid in examining patients who have a colostomy. This doughnut-shaped contrivance is placed over the colostomy and the rim is held firmly to the skin about the colostomy by suction from a water or electrically operated suction pump. Barium flows through the center of the doughnut-shaped device into the colon. Leakage of barium about the colostomy is thus prevented.—*C. A. Stevenson, M.D.*

Limperos, G., and Mosher, W. A. Protection of mice against x-radiation by thiourea. *Science*, July 21, 1950, *112*, 86–87.

Because thiourea has been found to protect the the depolymerization of desoxyribosenucleic acid (DNA) both *in vitro* and *in vivo*, it was postulated that the protection of such a vital cellular constituent might affect the mortality of roentgen irradiated animals.

Groups of mice were given a single dose of 650 r. Control groups, without thiourea, had a considerably higher mortality rate than the groups which received thiourea, either by injection or in their drinking water. As a result of these experiments, the authors believe that thiourea, and possibly other reducing agents, lower the mortality rate due to irradiation because of the protection of certain cellular constituents such as nucleic acid.—*J. W. Karr, M.D.*

Sokoloff, Boris, Redd, James B., and Dutcher, Raymond. Vitamin P protection against radiation. *Science*, July 28, 1950, *112*, 112–113.

This is a continuation study on flavanoid protection against radiation effects. Using rats as the experimental animal, control and experimental groups were given 800 r total body irradiation in a single exposure; 80 per cent of the control animals died within three weeks with the usual signs of hemorrhage and adrenal damage.

Two small groups of animals were given 40 to 150 mg. of vitamin P compound both before and after a similar dose of roentgen radiation. The survival rates of both groups were so much higher that it appears that the compound gives protection against radiation in rats.—*J. W. Karr, M.D.*

Cutler, Seymour S., Burbank, Benjamin, and Marzullo, Eugene R. Hypocoagulability of certain irradiated plasmas. *J.A.M.A.*, July 22, 1950, *143*, 1057–1059.

Sterilization of pooled human plasma has become necessary since some batches appear to transmit the virus causing homologous serum jaundice. Ultraviolet irradiation has been used for this purpose and it was believed that such treated plasma remained unchanged in chemical and electrophoretic behavior. However, the authors have found profound alterations of the clotting mechanism in some samples of irradiated plasma when a certain wavelength (namely, in the range of 2,537 angstrom units) was used. The use of this irradiated plasma causes a definite hypocoagulability.

The practical application of this knowledge appears to lie in the fact that patients suffering from the effect of an atomic accident who need large quantities of plasma will probably be potential candidates for hemorrhagic diatheses and as such would not be benefited by the administration of this plasma. However, there would be potential clinical value in this irradiated plasma as an anticoagulant.—*H. R. Fishback, Jr., M.D.*

Goldenberg, Marcel, and Aranow, Henry, Jr. Diagnosis of pheochromocytoma by the adrenergic blocking action of benzodioxan. *J.A.M.A.*, July 29, 1950, *143*, 1139–1143.

The authors refer to a previous report on the adrenergic blocking action of benzodioxan to demonstrate the presence of circulating epinephrine. Whereas pheochromocytomas responded with a drop of systolic and diastolic blood pressure, hypertension of other causation showed no change or a rise of blood pressure after intravenous administration of benzodioxan.

In experiments reported here, it is suggested that hypertension caused by the infusion of arterenol in man is much more susceptible to the blocking action of benzodioxan than would be anticipated from data obtained on animals.

Fifty-nine patients with operatively demonstrated pheochromocytomas showed positive response to the benzodioxan test, and only three false negative tests have been observed. This study consisted of 11 patients with a positive test and 1 with a negative test in the presence of pheochromocytoma. Details of test and discussion of reactions are given. The authors believe that the probable mechanism of a negative response to benzodioxan was due to a persistent hypertension associated with a pheochromocytoma.—*R. D. Moreton, M.D.*

Skipper, Howard E., Bell, Martelia J., and Chapman, Juanita B. Studies on the hazard involved in the use of C^{14}. II. The effect of a single dose of C^{14}-labeled sodiumbicarbonate on the pattern of deaths from spontaneous leukemia in Akm mice. *Cancer Research*, June, 1950, *10*, 362–363.

Carbon 14, in a form apt to be encountered in the laboratory ($NaHC^{14}O_3$), was injected into a strain of mice known to spontaneously develop leukemia (Akm strain). This was done to determine its effect on a malignancy known to be radiosensitive.

Each experimental mouse was given 18 microcuries

intraperitoneally, which is equivalent to 50 millicuries for a 70 kg. man. Over-all radiation from this dose in mice previously studied indicated an integrated exposure of about 0.11 r.e.p. for the first 24 hours and an average daily dose of about 0.003 r.e.p. for a period of 1 to 3 months.

No significant difference was seen in the pattern of leukemic death in the experimental as compared to the control animals.—*K. L. Krabbenhoft, M.D.*

Snyder, R. H., and Kisieleski, W. E. The relative biological effectiveness of beta and roentgen radiation as shown by the radiotoxicity of Na^{24} for mice. *Radiology*, May, 1950, *54*, 743–749.

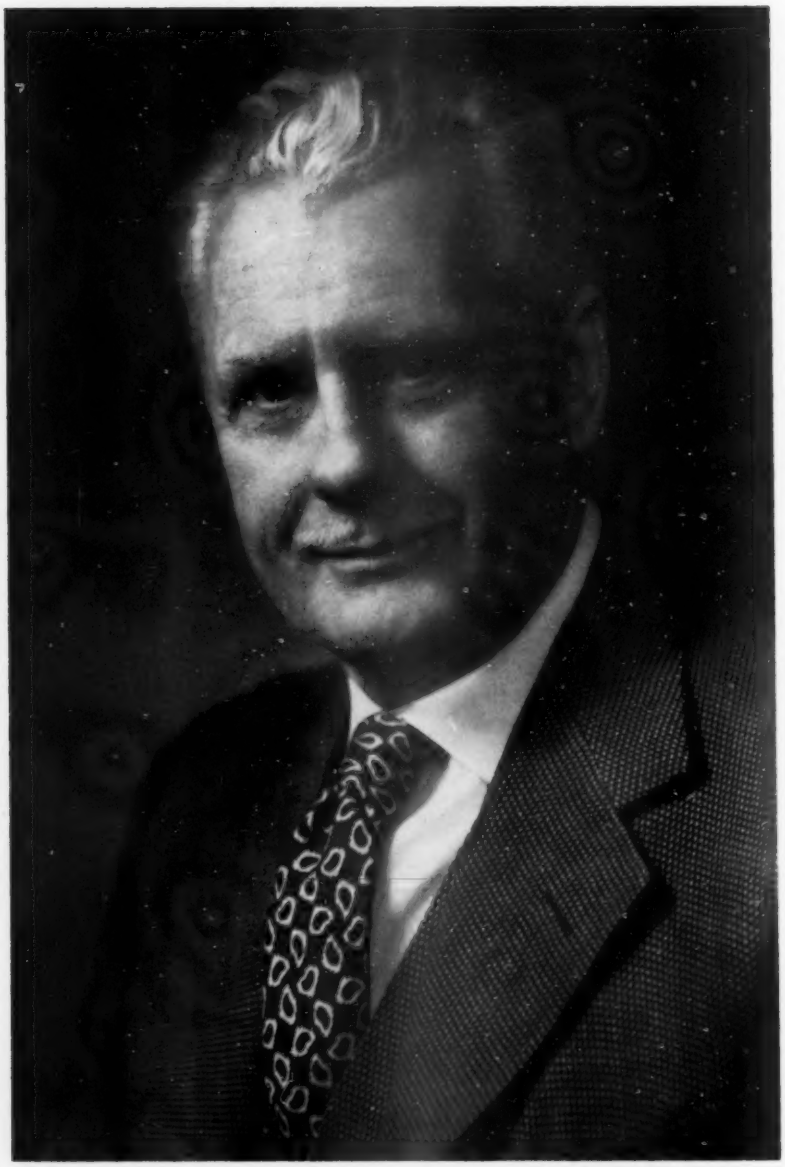
Another method of comparing the biological effect of beta and roentgen radiations is carried out by the authors utilizing total irradiation of mice. A twenty day LD_{50} (50 per cent mortality in 20 days) in mice is used as the death rate for comparison as compared to previous determinations on *Drosophila* eggs (Stapleton and Zirkle), lymphopenia in mice (Evans and Quimby), and inhibition of glycolysis in rat's retina (Crabtree and Gray). Na^{24}, which emits both beta and gamma rays is used as the beta-ray source because most of the gamma energy is dissipated outside the mice, and is fairly evenly distributed throughout the tissues. The experimental method and calculations necessary to determine the dose in rep per day (roentgen equivalent physical per day which approximates the roentgen used for roentgen rays) for Na^{24}, together with inherent errors in these methods, are very well discussed. It was found that the ratio of roentgen-ray (200 kv.) to beta-ray effectiveness is approximately 1.4:1. This compares favorably with 1.5 and 1.6 reported by Evans and Quimby, and Stapleton and Zirkle respectively (Evans and Quimby's figures corrected for the more recently determined value of average energy of the sodium beta). Henshaw's ratio of 1:1 is discussed and the authors believe the discrepancy may lie in the roentgen-ray dosage determination. A brief discussion is held on the possibility of obtaining a 1:1 ratio.—*M. B. Goodwin, M.D.*

Jennings, W. A. Physical aspects of the roentgen radiation from a beryllium window tube operated over the range 2–50 K.V.P. for clinical purposes. *Acta radiol.*, May, 1950, *33*, 435–484.

The relevant physical properties of low kilovoltage roentgen radiation are investigated with a view to clinical application. Using an AEG-50-T beryllium window tube, radiation generated over the range from 2 to 50 kv. (peak) at dosage rates up to 60,000 r per minute have been measured. A wide range of filtrations, field areas, focal skin distances and tube currents were used.

The paper is divided into two parts. The first one includes a description of the generating equipment and measuring apparatus, together with a discussion relating to the calibration. This covers all the radiation qualities and output rates concerned. The medium used for depth dose measurements is also considered.

The second part contains the experimental results. These relate to surface dosage rates and to the depth dosage. The ratio of the 90 per cent absorption depth to the half-value depth or "fall off" ratio is discussed. Data relating to the absorption of the radiation in aluminum are given and comparisons of the present results with other published work is made whenever possible.—*Mary Frances Vastine, M.D.*



Courtesy Fabian Bachrach

BERNARD PIERRE WIDMANN

President of the American Roentgen Ray Society, 1950–1951